

Supporting Information-I

Aminocatalytic asymmetric [4+2]-annulation to access functionally rich hexahydrospiroindole pyrazolones

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1. EXPERIMENTAL SECTION

1.1 General Experimental Procedures

Nuclear Magnetic Resonance Spectroscopy: ^1H NMR spectra were acquired on Bruker AVIII400 (400 MHz) spectrometer and were referenced to TMS and residual non-deuterated solvent peak in CDCl_3 ($\delta = 7.26$). Chemical shifts (δH and δC) are reported in parts per million (ppm), with signal splitting recorded as singlet (s), doublet (d), triplet (t), quartet (q), quintet (quint), and multiplet and unresolved peaks (m). Coupling constants (J) are mentioned in Hz and are presented as observed. ^{13}C NMR spectra were obtained on Bruker AVIII400 (100 MHz) spectrometers and were referenced to solvent peaks in CDCl_3 ($\delta = 77.0$). Where diastereomeric mixtures are formed, data is given for the major diastereomer.

Mass Spectrometry: High-resolution mass spectra (HRMS) were recorded by the Thermo Fisher spectrometer using electrospray ionization (ESI^+). The parent ion $[\text{M}+\text{H}]^+$ $[\text{M}+\text{Na}]^+$ is calculated to 4 decimal places from the molecular formula, and all values are within a tolerance of 5 ppm.

Specific rotations: Optical rotations were recorded on an Anton Parr MCP100 polarimeter with a path length of 1 dm (using the sodium D line, 589 nm). Specific rotations ($[\alpha]_D$) are reported in units of $10^{-1} \text{ deg cm}^2 \text{ g}^{-1}$. Concentrations are reported in g/mL. Temperatures are reported in $^\circ\text{C}$ (typically 25°C).

Infrared Spectroscopy: Absorption spectra were obtained on a Shimadzu FT-IR spectrometer. Wavelengths of maximum absorbance (ν_{max}) are quoted in wavenumbers (cm^{-1}). Only selected characteristic IR absorption data are provided for each compound.

Single Crystal XRD: Data was collected from Sophisticated Analytical Instrumental Facility, Indian Institute of Technology Madras- Chennai.

Materials:

Unless otherwise stated, all reactions were carried out in oven-dried glassware, using anhydrous reaction solvents. All other commercially available reagents and solvents were either used as received and/or dried and purified before use using standard procedures.

General Procedure A: Preparation of pyrrolidine-tethered dienal

1a-c were prepared by following the reported literature procedure.¹

General Procedure B: Preparation of pyrazolone olefins

2aa-2bw were synthesized using a literature report.² All the NMR's were consistent with the literature.

General Procedure C: Aminocatalytic [4+2]-annulation:

To an oven dried vial containing catalyst **3a** (0.2 equiv.), benzoic acid (0.2 equiv.) and the pyrazolone olefin (1.0 equiv.) was added the pyrrolidine-tethered dienal (1.2 equiv.) in toluene (0.13M). The resulting mixture was stirred at RT for 5-12 hours, the crude product was directly purified by column chromatography.

General Procedure D: Aminocatalytic [4+2]-annulation followed by one pot Wittig reaction:

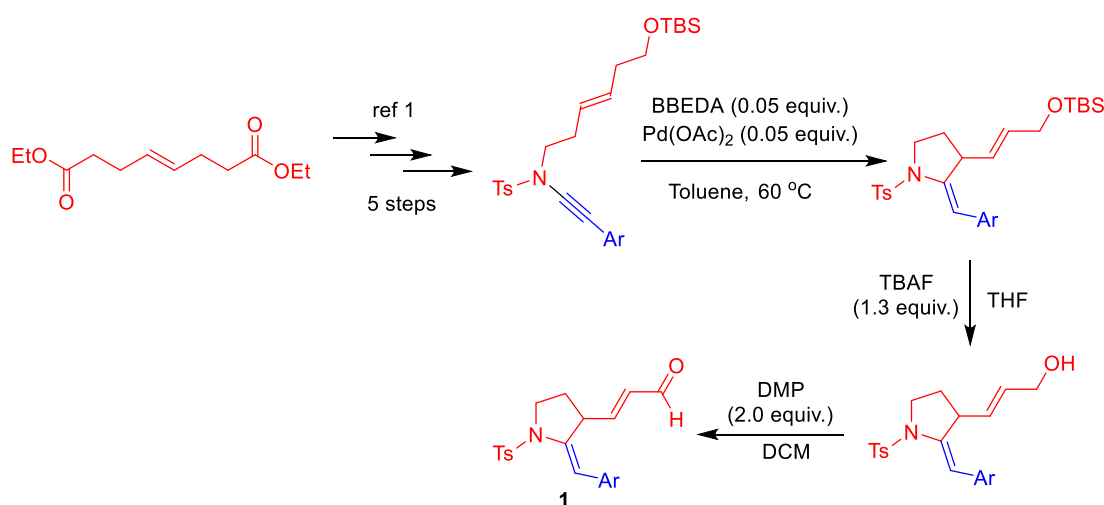
To an oven dried vial containing catalyst **3a** (0.2 equiv.), benzoic acid (0.2 equiv.) and the pyrazolone olefin (1.0 equiv.) was added the pyrrolidine-tethered dienal (1.2 equiv.) in toluene (0.13M). The resulting mixture was stirred at RT for 5-12 hours, then (ethoxycarbonylmethylene)triphenylphosphorane (0.15 mmol, 1.5 equiv.) was added. The reaction was then stirred for 2 hours, the crude product was directly purified by column chromatography.

General Procedure E: Ramachary Reductive Coupling (RRC) Reaction:

Into a glass vial L-proline (0.2 eq) was treated with product (-)-**4aaa** (1.0 eq), malononitrile (1.0 eq.) and Hantzsch ester (1.0 eq.) in DCM as a solvent. After the completion of the reaction crude mixture was purified using column chromatography and the resulting product (-)-**6aaa** was obtained as a yellow solid.³

General Procedure F: NaBH₄ reduction followed by fluoroetherification

Into a 10 ml RBF (-)-**4aaa** was taken in MeOH and NaBH₄ was added under N₂. After the completion of the reaction, the crude product was quenched using sat. NaHCO₃ solution and extracted with EtOAc. Then the concentrated material was treated with select fluor (F⁺ source) and NaHCO₃ in ACN yielded the fluorinated octahydrospiroindole pyrazolone (-)-**7aaa**.⁴

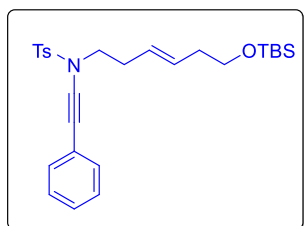
Synthetic Route of the Dienals (1a-1c)**References**

- 1) a) D. C. Braddock, R. Bhuvu, D. S. Millan, Y. Perez-Fuertes, C. A. Roberts, R. N. Shepperd, S. Solanki, E. S. E. Stokes, A. J. P. White, *Org. Lett.* 2007, **9**, 3, 445-448. b) V. Chintalapudi, E. A. Galvin, R. L. Greenaway, E. A. Anderson, *Chem. Commun.*, 2016, **52**, 693. c) A. Mekareeya, P. R. Walker, A. Couce-Rios, C. D. Campbell, A. Steven, R. S. Paton, E. A. Anderson, *J. Am. Chem. Soc.*, 2017, **139**, 10104–10114.
- 2) Y. Zhou, N. Chen, Y. Cheng, X. Cai, *J. Vis. Exp.*, 2019, **144**, 59155.
- 3) a) D. B. Ramachary and M. Kishor, *J. Org. Chem.*, 2007, **72**, 5056; (b) D. B. Ramachary and Y. V. Reddy, *J. Org. Chem.*, 2010, **75**, 74; (c) D. B. Ramachary and M. Kishor, *Org. Biomol. Chem.*, 2010, **8**, 2859 and references cited therein. d) D. B. Ramachary, M. A. Pasha, G. Thirupathi, *Angew. Chem., Int. Ed.*, 2017, **56**, 12930–12934.
- 4) a) O. Lozano, G. Blessley, T. M. D Campo, A. L. Thompson, G. T. Giuffredi, M. Bettati, M. Walker, R. Borman, V. R. Gouverneur, *Angew. Chem.*, 2011, **123**, 8255-8259

Characterization data

(E)-N-(6-((tert-butyldimethylsilyl)oxy)hex-3-en-1-yl)-4-methyl-N-(phenylethynyl)benzenesulfonamide:

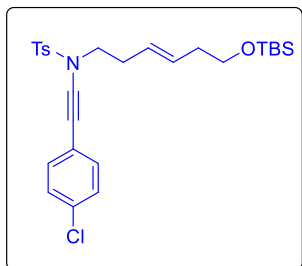
Prepared by following general procedure **A** purified by column chromatography using EtOAc/hexane



and isolated product in 59% yield as a pale-yellow liquid. IR (neat) ν_{\max} 2927, 2235, 1598, 1462, 1168, 1089 and 752. cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.83 (2H, d, $J = 8$ Hz), 7.37-7.33 (4H, m), 7.31-7.25 (3H, m), 5.54-5.34 (2H, m), 3.58 (2H, t, $J = 6.8$ Hz), 3.42 (2H, t, $J = 7.6$ Hz), 2.44 (3H, s), 2.39 (2H, q, $J = 6.8$ Hz), 2.17 (2H, q, $J = 6.8$ Hz), 0.88 (9H, s), 0.036 (6H, s); ^{13}C NMR (100 MHz, CDCl_3 , DEPT-135) δ 144.6 (C), 134.7 (C), 131.4 (2CH), 130.3 (CH), 129.8 (2CH), 128.3 (2CH), 127.8 (CH), 127.7 (2CH), 127.0 (CH), 122.9 (C), 82.3 (C), 70.9 (C), 63.0 (CH_2), 51.4 (CH_2), 36.3 (CH_2), 31.4 (CH_2), 26.0 (3 CH_3), 21.7 (CH_3), 18.4 (C), -5.22 (2 CH_3); HRMS (ESI) m/z : 484.2336 [$\text{M} + \text{H}$] $^+$, calcd for $\text{C}_{27}\text{H}_{38}\text{NO}_3\text{SSi}$; Found 484.2337.

(E)-N-(6-((tert-butyldimethylsilyl)oxy)hex-3-en-1-yl)-N-((4-chlorophenyl)ethynyl)-4-methylbenzenesulfonamide:

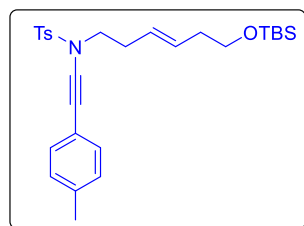
Prepared by following general procedure **A** purified by column chromatography using EtOAc/hexane



and isolated product in 56% yield as a pale-yellow liquid. IR (neat) ν_{\max} 2927, 2235, 1492, 1367, 1253, 1168, 1089 and 773. cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.81 (2H, d, $J = 8$ Hz), 7.35 (2H, d, $J = 8$ Hz), 7.30-7.24 (4H, m), 5.54-5.33 (2H, m), 3.58 (2H, t, $J = 6.8$ Hz), 3.41 (2H, t, $J = 7.2$ Hz), 2.45 (3H, s), 2.37 (2H, q, $J = 6.7$ Hz), 2.17 (2H, q, $J = 6.8$ Hz), 0.88 (9H, s), 0.035 (6H, s); ^{13}C NMR (100 MHz, CDCl_3 , DEPT-135) δ 144.7 (C), 143.6 (C), 133.7 (C), 132.5 (2CH), 130.7 (CH), 129.8 (2CH), 128.6 (2CH), 127.7 (2CH), 126.9 (CH), 121.4 (C), 83.2 (C), 70.0 (C), 62.9 (CH_2), 51.3 (CH_2), 36.3 (CH_2), 31.4 (CH_2), 26.0 (3 CH_3), 21.7 (CH_3), 18.4 (C), -5.23 (2 CH_3); HRMS (ESI) m/z : 540.1766 [$\text{M} + \text{Na}$] $^+$, calcd for $\text{C}_{27}\text{H}_{36}\text{NO}_3\text{ClNaSSi}$; Found 540.1778.

(E)-N-(6-((tert-butyldimethylsilyl)oxy)hex-3-en-1-yl)-4-methyl-N-(p-tolyethynyl)benzenesulfonamide:

Prepared by following general procedure **A** purified by column chromatography using EtOAc/hexane

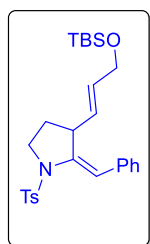


and isolated product in 53% yield as a pale-yellow liquid. IR (neat) ν_{\max} 2927, 1597, 1367, 1168, 1089 and 812. cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.83 (2H, d, $J = 8$ Hz), 7.34 (2H, d, $J = 8.4$ Hz), 7.26 (2H, d, $J = 8$ Hz), 7.09 (2H, d, $J = 8$ Hz), 5.54-5.34 (2H, m), 3.58 (2H, t, $J = 6.8$ Hz), 3.40 (2H, t, $J = 7.6$ Hz), 2.44 (3H, s), 2.38 (2H, q, $J = 7.2$ Hz), 2.34 (3H, s), 2.17 (2H, q, $J = 6.8$ Hz), 0.88 (9H, s), 0.035 (6H, s); ^{13}C NMR (100 MHz, CDCl_3 ,

DEPT-135) δ 144.5 (C), 138.0 (C), 134.7 (C), 131.5 (2CH), 130.2 (CH), 129.7 (2CH), 129.0 (2CH), 127.7 (2CH), 127.1 (CH), 119.7 (C), 81.5 (C), 70.8 (C), 63.0 (CH₂), 51.4 (CH₂), 36.3 (CH₂), 31.3 (CH₂), 26.0 (3CH₃), 21.7 (CH₃), 21.5 (CH₃), 18.4 (C), -5.23 (2CH₃); HRMS (ESI) m/z : 520.2312 [M + Na]⁺, calcd for C₂₈H₃₉NO₃NaSSi; Found 520.2313.

2-((*E*-benzylidene)-3-((*E*-3-((*tert*-butyldimethylsilyl)oxy)prop-1-en-1-yl)-1-tosylpyrrolidine:

Prepared by following general procedure **A** purified by column chromatography using EtOAc/hexane

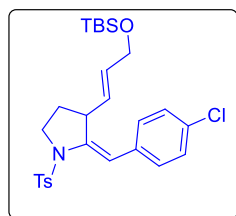


and isolated product in 84% yield as a pale-yellow liquid. IR (neat) ν_{\max} 2953, 1597, 1359, 1163, 1089 and 833. cm⁻¹; ¹H NMR (400 MHz, CDCl₃ 5.5:1 ratio of isomers, major isomer) δ 7.65 (2H, d, J = 8.2 Hz), 7.62 (2H, d, J = 7.4 Hz), 7.34-7.26 (4H, m), 7.19 (1H, q, J = 7.4 Hz), 5.92 (1H, d, J = 2 Hz), 5.51 (1H, dt, J = 4.9, 15.3 Hz), 5.34 (1H, dd, J = 8.4, 8.4 Hz), 4.14 (2H, dd, J = 1.4, 3.5 Hz), 3.73-3.66 (1H, m), 3.56-3.49 (1H, m), 2.57 (1H, q, J = 8.4 Hz), 2.43 (3H, s), 1.84-1.77 (1H, m), 1.48-1.37 (1H, m), 0.91 (9H, s), 0.08

(6H, s); ¹³C NMR (100 MHz, CDCl₃, DEPT-135) δ 144.1 (C), 140.8 (C), 136.5 (C), 134.6 (C), 132.8 (CH), 129.6 (2CH), 129.3 (CH), 129.0 (2CH), 128.1 (2CH), 127.9 (2CH), 127.0 (CH), 119.0 (CH), 63.5 (CH₂), 49.3 (CH₂), 46.4 (CH), 29.0 (CH₂), 26.1 (3CH₃), 21.7 (CH₃), 18.6 (C), -4.99 (2CH₃); HRMS (ESI) m/z : 506.2156 [M + Na]⁺, calcd for C₂₇H₃₇NO₃NaSSi; Found 506.2156.

3-((*E*-3-((*tert*-butyldimethylsilyl)oxy)prop-1-en-1-yl)-2-((*E*-4-chlorobenzylidene)-1-tosylpyrrolidine:

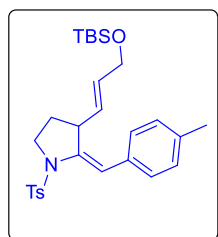
Prepared by following general procedure **A** purified by column chromatography using EtOAc/hexane



and isolated product in 80% yield as a pale-yellow liquid. IR (neat) ν_{\max} 2927, 1597, 1359, 1251, 1165, 1089 and 835. cm⁻¹; ¹H NMR (400 MHz, CDCl₃, 8.5:1 ratio of isomers, major isomer) δ 7.63 (2H, d, J = 8.2 Hz), 7.53 (2H, d, J = 8.5 Hz), 7.27 (2H, d, J = 8.5 Hz), 7.22 (1H, d, J = 8.5 Hz), 5.86 (1H, d, J = 2 Hz), 5.52 (1H, dt, J = 2.2, 15.2 Hz), 5.33 (1H, dd, J = 8.4, 8.4 Hz), 4.14 (2H, dd, J = 1.4, 3.4 Hz), 3.73-3.67 (1H, m), 3.56-3.49 (1H, m), 2.57 (1H, q, J = 8.3 Hz), 2.43

(3H, s), 1.85-1.77 (1H, m), 1.47-1.37 (1H, m), 0.91 (9H, s), 0.07 (6H, s); ¹³C NMR (100 MHz, CDCl₃, DEPT-135) δ 144.2 (C), 141.5 (C), 134.9 (C), 134.4 (C), 132.9 (CH), 132.2 (C), 130.2 (2CH), 129.6 (2CH), 128.9 (CH), 127.9 (2CH), 127.9 (2CH), 117.5 (CH), 63.3 (CH₂), 49.3 (CH₂), 46.4 (CH), 28.8 (CH₂), 26.0 (3CH₃), 21.6 (CH₃), 18.5 (C), -5.1 (2CH₃); HRMS (ESI) m/z : 518.1947 [M + H]⁺, calcd for C₂₇H₃₇NO₃ClSSi; Found 518.1945.

3-((*E*-3-((*tert*-butyldimethylsilyl)oxy)prop-1-en-1-yl)-2-((*E*-4-methylbenzylidene)-1-tosylpyrrolidine:

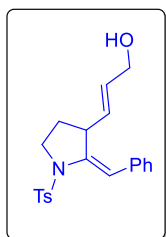


Prepared by following general procedure **A** purified by column chromatography using EtOAc/hexane and isolated product in 78% yield as a pale-yellow liquid. IR (neat) ν_{\max} 2924, 1462, 1361, 1251, 1166, 1089 and 835. cm⁻¹; ¹H NMR (400 MHz, CDCl₃, 6.5:1 ratio of isomers, major isomer) δ 7.66 (2H, d, J = 8.2 Hz), 7.53 (2H, d, J = 8.0 Hz), 7.27 (2H, d, J = 8.8 Hz), 7.09 (2H, d, J = 8 Hz), 5.9 (1H, d, J = 1.9

Hz), 5.5 (1H, dt, $J = 5.0, 15.2$ Hz), 5.33 (1H, dd, $J = 8.4, 8.4$ Hz), 4.14 (2H, dd, $J = 1.4, 3.6$ Hz), 3.72-3.66 (1H, m), 3.56-3.49 (1H, m), 2.54 (1H, q, $J = 8.4$ Hz), 2.43 (3H, s), 2.32 (3H, s), 1.82-1.75 (1H, m), 1.46-1.35 (1H, m), 0.91 (9H, s), 0.07 (6H, s); ^{13}C NMR (100 MHz, CDCl_3 , DEPT-135) δ 143.9 (C), 139.8 (C), 136.6 (C), 134.6 (C), 133.4 (C), 132.5 (CH), 129.5 (2CH), 129.4 (CH), 128.8 (2CH), 128.5 (2CH), 128.0 (2CH), 119.0 (CH), 63.4 (CH_2), 49.2 (CH_2), 46.2 (CH), 28.9 (CH_2), 26.0 (3CH_3), 21.6 (CH_3), 21.4 (CH_3), 18.5 (C), -5.1 (2CH_3); HRMS (ESI) m/z : 520.2312 $[\text{M} + \text{Na}]^+$, calcd for $\text{C}_{28}\text{H}_{39}\text{NO}_3\text{NaSSi}$; Found 520.2314.

(E)-3-(2-((E)-benzylidene)-1-tosylpyrrolidin-3-yl)prop-2-en-1-ol:

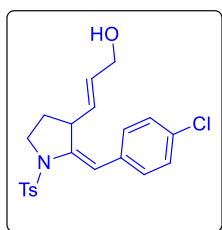
Prepared by following general procedure **A** purified by column chromatography using EtOAc/hexane



and isolated product in 90% yield as a pale-yellow liquid. IR (neat) ν_{max} 3412, 2956, 1597, 1354, 1159, 1087 and 657. cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.63 (2H, d, $J = 8.2$ Hz), 7.60 (2H, d, $J = 7.4$ Hz), 7.29-7.25 (4H, m), 7.17 (1H, t, $J = 7.4$ Hz), 5.92 (1H, d, $J = 1.84$ Hz), 5.58 (1H, dt, $J = 5.6, 15.3$ Hz), 5.35 (1H, dd, $J = 8.4, 8.4$ Hz), 4.09 (2H, d, $J = 5.5$ Hz), 3.69 (1H, dd, $J = 3.1, 8.5$), 3.56-3.49 (1H, m), 2.6 (1H, q, $J = 8.4$ Hz), 2.42 (3H, s), 1.96-1.77 (2H, m), 1.49-1.39 (1H, m); ^{13}C NMR (100 MHz, CDCl_3 , DEPT-135) δ 144.1 (C), 140.4 (C), 136.3 (C), 134.4 (C), 132.1 (CH), 130.7 (CH), 129.5 (2CH), 128.8 (2CH), 127.9 (2CH), 127.8 (2CH), 126.9 (CH), 118.9 (CH), 63.0 (CH_2), 49.2 (CH_2), 46.2 (CH), 28.8 (CH_2), 21.6 (CH_3); HRMS (ESI) m/z : 392.1291 $[\text{M} + \text{Na}]^+$, calcd for $\text{C}_{21}\text{H}_{23}\text{NO}_3\text{NaS}$; Found 392.1290.

(E)-3-(2-((E)-4-chlorobenzylidene)-1-tosylpyrrolidin-3-yl)prop-2-en-1-ol:

Prepared by following general procedure **A** purified by column chromatography using EtOAc/hexane



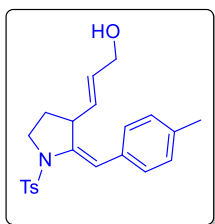
and isolated product in 85% yield as a pale yellow liquid. IR (neat) ν_{max} 3422, 2926, 1597, 1352, 1161, 1087 and 813. cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.62 (2H, d, $J = 8.2$ Hz), 7.52 (2H, d, $J = 8.5$ Hz), 7.27 (2H, d, $J = 8.2$ Hz), 7.22 (2H, d, $J = 8.5$ Hz), 5.86 (1H, d, $J = 1.92$ Hz), 5.6 (1H, dt, $J = 5.5, 15.3$ Hz), 5.35 (1H, dd, $J = 8.5, 8.5$ Hz), 4.11 (2H, d, $J = 5.5$ Hz), 3.74-3.68 (1H, m), 3.57-3.5 (1H, m), 2.61 (1H, q, $J = 8.3$ Hz), 2.43 (3H, s), 1.86-1.79 (1H, m), 1.69 (1H, br s), 1.50-

1.39 (1H, m); ^{13}C NMR (100 MHz, CDCl_3 , DEPT-135) δ 144.3 (C), 141.2 (C), 134.9 (C), 134.4 (C), 132.3 (CH), 132.3 (C), 130.4 (CH), 130.1 (2CH), 129.6 (2CH), 127.9 (2CH), 127.9 (2CH), 117.5 (CH), 63.0 (CH_2), 49.3 (CH_2), 46.4 (CH), 28.8 (CH_2), 21.6 (CH_3); HRMS (ESI) m/z : 426.0901 $[\text{M} + \text{Na}]^+$, calcd for $\text{C}_{21}\text{H}_{22}\text{NO}_3\text{ClNaS}$; Found 426.0907.

(E)-3-(2-((E)-4-methylbenzylidene)-1-tosylpyrrolidin-3-yl)prop-2-en-1-ol:

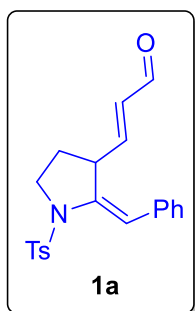
Prepared by following general procedure **A** purified by column chromatography using EtOAc/hexane

and isolated product **c** in 79% yield as a pale-yellow liquid. IR (neat) ν_{max} 3398, 2922, 1597, 1352, 1159, 1087 and 812. cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.65 (2H, d, $J = 8.2$ Hz), 7.51 (2H, d, $J = 8.04$ Hz), 7.27 (2H, d, $J = 7.6$ Hz), 7.09 (2H, d, $J = 8$ Hz), 5.89 (1H, d, $J = 1.52$ Hz), 5.57 (1H, dt, $J = 5.6, 15.3$ Hz), 5.35 (1H, dd, $J = 8.5, 8.5$ Hz), 4.10 (2H, d, $J = 5.22$ Hz), 3.73-3.67 (1H, m), 3.59-3.49 (1H, m), 2.58 (1H, q, $J = 8.4$ Hz), 2.42 (3H, s), 2.32 (3H, s), 1.98 (1H, br s), 1.83-1.76 (1H, m), 1.48-1.38 (1H, m); ^{13}C



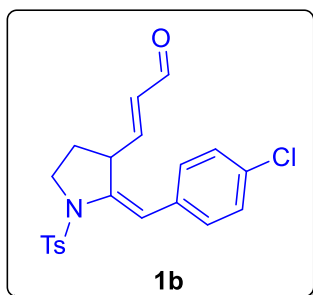
NMR (100 MHz, CDCl_3 , DEPT-135) δ 144.0 (C), 139.6 (C), 136.7 (C), 134.5 (C), 133.3 (C), 131.9 (CH), 131.0 (CH), 129.5 (2CH), 128.8 (2CH), 128.5 (2CH), 128.0 (2CH), 119.1 (CH), 63.1 (CH_2), 49.2 (CH_2), 46.2 (CH) 28.9 (CH_2), 21.6 (CH_3) 21.4 (CH_3); HRMS (ESI) m/z : 406.1447 [$\text{M} + \text{Na}$] $^+$, calcd for $\text{C}_{22}\text{H}_{25}\text{NO}_3\text{NaS}$; Found 406.1451.

(E)-3-(2-((E)-benzylidene)-1-tosylpyrrolidin-3-yl)acrylaldehyde (1a):



Prepared by following general procedure **A** purified by column chromatography using ether/hexane and isolated product **1a** in 80% yield as a pale-yellow semi solid. IR (neat) ν_{max} 2976, 1687, 1595, 1354, 1161, 1087 and 817. cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 9.45 (1H, d, $J = 7.8$ Hz), 7.65 (2H, d, $J = 8.24$ Hz), 7.58 (2H, d, $J = 7.4$ Hz), 7.26-7.20 (4H, m), 7.20 (1H, t, $J = 7.32$ Hz), 6.39 (1H, dd, $J = 8.8$, 8.8 Hz), 6.03 (1H, dd, $J = 7.8$, 7.8 Hz), 5.91 (1H, d, $J = 1.56$ Hz), 3.84-3.78 (1H, m), 3.64 (1H, dt, $J = 7.9$, 11.96 Hz), 3.04 (1H, q, $J = 8.6$ Hz), 2.43 (3H, s), 1.97-1.89 (1H, m), 1.58 (1H, dq, $J = 8.6$, 8.6 Hz); ^{13}C NMR (100 MHz, CDCl_3 , DEPT-135) δ 193.3 (C, H-C=O), 155.2 (CH), 144.6 (C), 138.5 (C), 135.7 (C), 134.5 (C), 133.8 (CH), 129.8 (2CH), 129.0 (2CH), 128.1 (2CH), 128.0 (2CH), 127.5 (CH), 120.8 (CH), 49.8 (CH_2), 46.6 (CH) 28.5 (CH_2), 21.7 (CH_3); HRMS (ESI) m/z : 390.1134 [$\text{M} + \text{Na}$] $^+$, calcd for $\text{C}_{21}\text{H}_{22}\text{NO}_3\text{NaS}$; Found 390.1135.

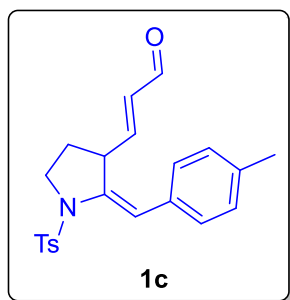
(E)-3-(2-((E)-4-chlorobenzylidene)-1-tosylpyrrolidin-3-yl)acrylaldehyde (1b):



Prepared by following general procedure **A** purified by column chromatography using ether/hexane and isolated product **1b** in 70% yield as a yellow semi solid. IR (neat) ν_{max} 2924, 1683, 1597, 1489, 1354, 1161, 1087 and 813. cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 9.46 (1H, d, $J = 7.8$ Hz), 7.63 (2H, d, $J = 8.24$ Hz), 7.50 (2H, d, $J = 8.52$ Hz), 7.29 (2H, d, $J = 8.1$ Hz), 7.23 (2H, d, $J = 8.5$ Hz), 6.39 (1H, dd, $J = 8.8$, 8.8 Hz), 6.04 (1H, dd, $J = 7.8$, 7.8 Hz), 5.85 (1H, d, $J = 1.68$ Hz), 3.87-3.80 (1H, m), 3.65 (1H, dt, $J = 7.7$, 11.96 Hz), 3.05 (1H, q, $J = 8.6$ Hz), 2.44 (3H, s), 2.0-1.92 (1H, m), 1.6 (1H, dq, $J = 8.5$, 8.5 Hz); ^{13}C NMR (100 MHz, CDCl_3 , DEPT-135) δ 193.1 (C, H-C=O), 154.7 (C), 144.7 (C), 139.2 (C), 134.4 (C), 134.1 (C), 133.9 (CH), 130.1 (2CH), 129.8 (2CH), 128.1 (2CH), 127.9 (2CH), 119.3 (CH), 116.5 (CH), 49.8 (CH_2), 46.6 (CH) 28.4 (CH_2), 21.7 (CH_3); HRMS (ESI) m/z : 424.0745 [$\text{M} + \text{Na}$] $^+$, calcd for $\text{C}_{21}\text{H}_{20}\text{NO}_3\text{NaS}$; Found 424.0750.

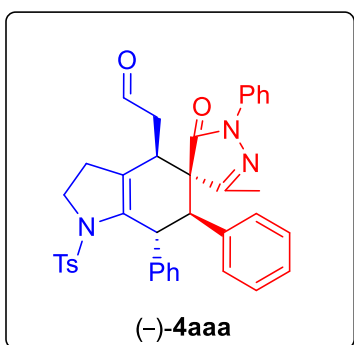
(E)-3-(2-((E)-4-methylbenzylidene)-1-tosylpyrrolidin-3-yl)acrylaldehyde (1c):

Prepared by following general procedure **A** purified by column chromatography using ether/hexane and isolated product **1c** in 62% yield as a yellow semi solid. IR (neat) ν_{max} 2924, 1674, 1598, 1352, 1161, 1087 and 812. cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 9.45 (1H, d, $J = 7.8$ Hz), 7.66 (2H, d, $J = 8.2$ Hz), 7.50 (2H, d, $J = 8.04$ Hz), 7.28 (2H, d, $J = 8.2$ Hz), 7.1 (2H, d, $J = 8$ Hz), 6.38 (1H, dd, $J = 8.8$, 8.8 Hz), 6.01 (1H, dd, $J = 7.8$, 7.8 Hz), 5.89 (1H, br s), 3.85-3.79 (1H, m), 3.65 (1H, dt, $J = 7.8$, 11.96 Hz), 3.01 (1H, q, $J = 8.6$ Hz), 2.44 (3H, s), 2.33 (3H, s), 1.96-1.84 (1H, m), 1.58-1.52 (1H, m); ^{13}C NMR (100 MHz,



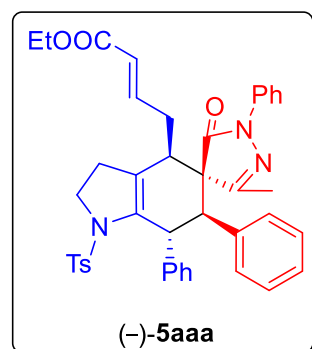
CDCl₃, DEPT-135) δ 193.2 (C, H-C=O), 155.3 (CH), 144.4 (C), 137.6 (C), 134.5 (C), 133.7 (CH), 132.6 (C), 129.7 (2CH), 128.8 (2CH), 128.6 (2CH), 128.0 (2CH), 120.9 (CH), 49.7 (CH₂), 46.4 (CH), 28.4 (CH₂), 21.6 (CH₃), 21.4 (CH₃); HRMS (ESI) m/z : 404.1291 [M + Na]⁺, calcd for C₂₂H₂₃NO₃NaS; Found 404.1294.

2-((4*R*,5*R*,6*R*,7*R*)-3'-methyl-5'-oxo-1',6,7-triphenyl-1-tosyl-1',2,3,4,5',6,7-octahydrospiro[indole-5,4'-pyrazol]-4-yl)acetaldehyde (4aaa):



Prepared by following general procedure **C** purified by column chromatography using EtOAc/hexane and isolated product **4aaa** in 85% yield as a yellow solid with M. P. 102-105 °C. The enantiomeric excess (ee) was determined by chiral stationary phase HPLC using a Daicel Chiralpak IC column (hexane/EtOAc = 70:30, flow rate 1 mL/min, λ = 254 nm), t_R = 7.365 min (major), t_R = 8.182 min (minor); $[\alpha]_D^{25}$ = -161.111 (CHCl₃, c = 0.72 g/100mL for 96% ee); IR (neat) ν_{\max} 2922, 1718, 1695, 1595, 1159 and 752. cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 9.62 (1H, s), 8.14 (2H, d, J = 8.2 Hz), 7.83 (2H, d, J = 7.7 Hz), 7.44 (2H, d, J = 8.3 Hz), 7.33 (2H, d, J = 8.1 Hz), 7.24 (1H, t, J = 7.4 Hz), 7.08-6.87 (10H, m), 4.84 (1H, d, J = 10.1 Hz), 3.74-3.58 (3H, m), 3.13 (1H, d, J = 10.5 Hz), 2.45 (3H, s), 2.38 (1H, dd, J = 9.2, 9.2 Hz), 2.03 (1H, dd, J = 3.2, 3.2 Hz), 1.98 (3H, s), 1.90 (1H, dd, J = 9.3, 9.3 Hz), 1.65-1.63 (1H, m); ¹³C NMR (100 MHz, CDCl₃, DEPT-135) δ 190.0 (C, H-C=O), 172.4 (C, N-C=O), 160.7 (C, C=N), 143.5 (C), 140.4 (C), 137.6 (C), 136.7 (C), 134.6 (C), 129.3 (2CH), 128.9 (4CH), 128.8 (2CH), 128.4 (2CH), 127.8 (5CH), 126.3 (CH), 125.9 (C), 125.4 (CH), 119.1 (3CH), 61.1 (C), 55.8 (CH), 49.6 (CH₂), 44.7 (CH), 42.3 (CH₂), 33.7 (CH), 30.4 (CH₂), 21.7 (CH₃), 13.9 (CH₃); HRMS (ESI) m/z : 652.2241 [M + Na]⁺, calcd for C₃₈H₃₅N₃O₄SNa; Found 652.2241.

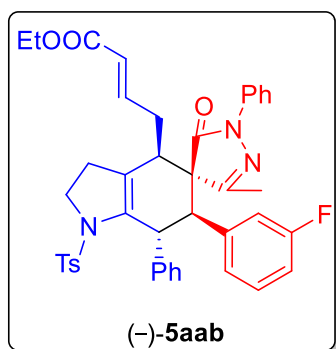
Ethyl(E)-4-((4*R*,5*R*,6*S*,7*S*)-3'-methyl-5'-oxo-1',6,7-triphenyl-1-tosyl-1',2,3,4,5',6,7-octahydrospiro[indole-5,4'-pyrazol]-4-yl)but-2-enoate (5aaa):



Prepared by following general procedure **D** purified by column chromatography using EtOAc/hexane and isolated product **5aaa** in 85% yield as a yellow solid with M. P. 102 °C. The enantiomeric excess (ee) was determined by chiral stationary phase HPLC using a Daicel Chiralpak IC column (hexane/EtOAc = 70:30, flow rate 1.0 mL/min, λ = 254 nm), t_R = 7.571 min (major), t_R = 9.605 min (minor), $[\alpha]_D^{25}$ = -105.268 (CHCl₃, c = 0.12 g/100mL, CHCl₃ for 96% ee); IR (neat) ν_{\max} 2926, 1699, 1597, 1454, 1157 and 750.31 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 8.21 (2H, d, J = 8.4 Hz), 7.79 (2H, d, J = 8.4 Hz), 7.43-7.37 (4H, m), 7.22 (1H, t, J = 7.2 Hz), 7.07-6.98 (7H, m), 6.87 (2H, d, J = 6.8 Hz), 6.72 (1H, quin, J = 7.2 Hz), 5.62 (1H, d, J = 15.6 Hz), 4.86 (1H, d, J = 10 Hz), 4.15-

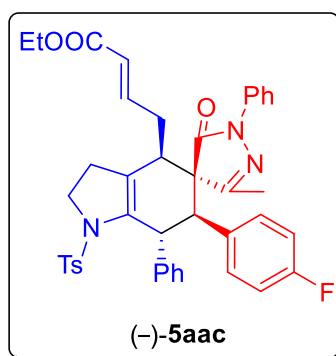
4.03 (2H, m), 3.71 (1H, dd, $J = 7.6, 7.2$ Hz), 3.60 (1H, ddd, $J = 9.2, 9.2, 9.2$ Hz), 3.14 (1H, m), 3.07 (1H, d, $J = 10.4$ Hz), 2.46 (3H, s), 2.17 (1H, quin, $J = 7.2$ Hz), 2.05-2.02 (1H, m), 2.00 (3H, s), 1.98-1.92 (1H, m), 1.79-1.67 (2H, m), 1.21 (3H, t, $J = 6.8$ Hz); ^{13}C NMR (100 MHz, CDCl_3 , DEPT-135) δ 172.1 (C, O-C=O), 165.7 (C, N-C=O), 160.4 (C, C=N), 144.9 (2CH), 143.7 (2C), 140.5 (2C), 140.4 (2C), 137.6 (C), 136.5 (C), 134.3 (C), 129.5 (3CH), 128.8 (4CH), 128.3 (CH), 127.7 (3CH), 127.1 (C), 126.2 (CH), 125.2 (C), 123.9 (C), 119.2 (3CH), 61.4 (C), 60.4 (CH_2), 56.2 (CH), 50.0 (CH_2), 44.5 (CH), 40.0 (CH), 31.9 (CH_2), 30.9 (CH_2), 22.6 (CH_3), 14.1 (CH_3), 14.0 (CH_3); HRMS (ESI) m/z : 722.2659 $[\text{M} + \text{Na}]^+$, calcd for $\text{C}_{42}\text{H}_{41}\text{N}_3\text{O}_5\text{SNa}$; Found 722.2683.

Ethyl(*E*)-4-((4*R*,5*R*,6*S*,7*S*)-6-(3-fluorophenyl)-3'-methyl-5'-oxo-1',7-diphenyl-1-tosyl-1,1',2,3,4,5',6,7-octahydrospiro[indole-5,4'-pyrazol]-4-yl)but-2-enoate (5aab**):**



Prepared by following general procedure **D** purified by column chromatography using EtOAc/hexane and isolated product **5a**ab**** in 66% yield as a yellow solid with M. P. 120-123 °C. The enantiomeric excess (ee) was determined by chiral stationary phase HPLC using a Daicel Chiralpak IC column (hexane/EtOAc = 70:30, flow rate 0.5 mL/min, $\lambda = 254$ nm), $t_R = 13.949$ min (major), $t_R = 17.717$ min (minor), $[\alpha]_D^{25} = -167.583$ (CHCl_3 , $c = 0.12$ g/100mL for 97% ee); IR (neat) ν_{max} 2924, 1699, 1595, 1490, 1452, 1348 and 1159 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 8.20 (2H, d, $J = 8.2$ Hz), 7.79 (2H, d, $J = 7.5$ Hz), 7.44-7.37 (4H, m), 7.22 (1H, t, $J = 7.4$ Hz), 7.11-7.04 (3H, m), 6.98 (1H, q, $J = 6.6$ Hz), 6.88 (2H, d, $J = 6.2$ Hz), 6.78-6.64 (3H, m), 5.62 (1H, d, $J = 15.48$ Hz), 4.83 (1H, d, $J = 10.4$ Hz), 4.15-4.03 (2H, m), 3.73-3.54 (2H, m), 3.14 (1H, br s), 3.07 (1H, d, $J = 10.5$ Hz), 2.46 (3H, s), 2.16 (1H, quin $J = 7.1$ Hz), 2.05-2.02 (1H, m), 2.0 (3H, s), 1.98-1.90 (1H, m), 1.78-1.68 (2H, m), 1.20 (3H, t, $J = 7.1$ Hz); ^{13}C NMR (100 MHz, CDCl_3 , DEPT-135) δ 171.9 (C, O-C=O), 165.6 (C, N-C=O), 160.2 (C, C=N), 144.6 (2CH), 143.7 (C), 140.2 (C), 140.1 (C), 137.5 (C), 134.3 (C), 129.8 (C), 129.5 (3CH), 128.8 (3CH, d, $J = 8$ Hz), 127.9 (3CH), 127.3 (2CH), 126.5 (2CH), 125.4 (2CH), 124.0 (2CH), 119.2 (3CH), 114.8 (CH, d, $J = 21$ Hz), 61.2 (C), 60.4 (CH_2), 55.8 (CH), 50.0 (CH_2), 44.5 (CH), 39.9 (CH), 31.9 (CH_2), 30.9 (CH_2), 21.6 (CH_3), 14.2 (CH_3), 14.0 (CH_3); HRMS (ESI) m/z : 740.2565 $[\text{M} + \text{Na}]^+$, calcd for $\text{C}_{42}\text{H}_{40}\text{FN}_3\text{O}_5\text{SNa}$; Found 740.2558.

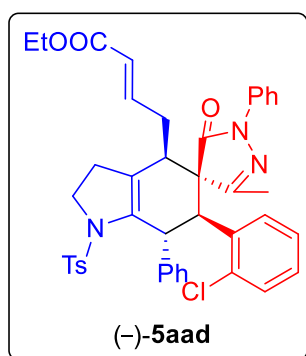
Ethyl(*E*)-4-((4*R*,5*R*,6*S*,7*S*)-6-(4-fluorophenyl)-3'-methyl-5'-oxo-1',7-diphenyl-1-tosyl-1,1',2,3,4,5',6,7-octahydrospiro[indole-5,4'-pyrazol]-4-yl)but-2-enoate (5ac**):**



Prepared by following general procedure **D** purified by column chromatography using EtOAc/hexane and isolated product **5a**c**** in 68% yield as a pale-yellow solid with M. P. 89-91 °C. The enantiomeric excess (ee) was determined by chiral stationary phase HPLC using a Daicel Chiralpak IC column (hexane/EtOAc = 70:30, flow rate 0.5 mL/min, $\lambda = 254$ nm), $t_R = 14.529$ min (major), $t_R = 19.923$ min (minor), $[\alpha]_D^{25} = -108.333$ (CHCl_3 , $c = 0.3$ g/100mL for 96% ee); IR (neat) ν_{max} 2924, 1716, 1597, 1496, 1365, 1157 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 8.19 (2H, d, $J = 8.2$ Hz), 7.80 (2H, d, $J = 7.6$ Hz), 7.43 (2H, t, $J = 8.5$ Hz), 7.38 (2H, d, $J = 8.0$ Hz),

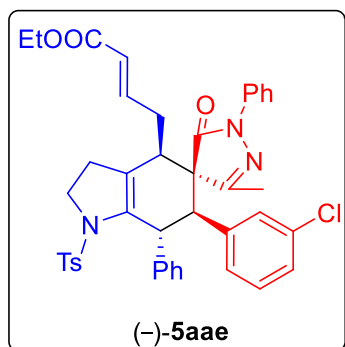
7.23 (1H, t, $J = 7.4$ Hz), 7.10-7.04 (3H, m), 6.86 (3H, d, $J = 6.1$ Hz), 6.73-6.65 (3H, m), 5.62 (1H, d, $J = 15.5$ Hz), 4.81-4.79 (1H, m), 4.15-4.04 (2H, m), 3.74-3.55 (2H, m), 3.14 (1H, br s), 3.07 (1H, d, $J = 10.6$ Hz), 2.46 (3H, s), 2.18 (1H, quin, $J = 7.4$ Hz), 2.05-2.02 (1H, m), 1.99 (3H, s), 1.96-1.92 (1H, m), 1.81-1.71 (2H, m), 1.20 (3H, t, $J = 7.1$ Hz); ^{13}C NMR (100 MHz, CDCl_3 , DEPT-135) δ 172.0 (C, O-C=O), 165.6 (C, N-C=O), 162.1 (C, d, $J = 245$ Hz), 160.2 (C, C=N), 144.6 (2CH), 143.7 (C), 140.3 (C), 140.2 (C), 137.5 (C), 134.3 (C), 129.5 (3CH), 128.8 (4CH, d, $J = 11$ Hz), 127.9 (3CH), 127.1 (C), 126.4 (2CH), 125.4 (2CH), 124.0 (2CH), 119.0 (3CH), 115.2 (CH, d, $J = 21$ Hz), 61.4 (C), 60.4 (CH_2), 55.4 (CH), 50.0 (CH_2), 44.7 (CH), 39.9 (CH), 31.9 (CH_2), 30.9 (CH_2), 21.6 (CH_3), 14.2 (CH_3), 14.0 (CH_3); HRMS (ESI) m/z : 740.25649 $[\text{M} + \text{Na}]^+$, calcd for $\text{C}_{42}\text{H}_{40}\text{FN}_3\text{O}_5\text{SNa}$; Found 740.25653.

Ethyl(*E*)-4-((4*R*,5*R*,6*R*,7*S*)-6-(2-chlorophenyl)-3'-methyl-5'-oxo-1',7-diphenyl-1-tosyl-1,1',2,3,4,5',6,7-octahydrospiro[indole-5,4'-pyrazol]-4-yl)but-2-enoate (5aad):



Prepared by following general procedure **D** purified by column chromatography using EtOAc/hexane and isolated product **5aad** in 83% yield as a Off white solid with M. P. 124-127 °C. The enantiomeric excess (ee) was determined by chiral stationary phase HPLC using a Daicel Chiralpak IC column (hexane/EtOAc = 70:30, flow rate 0.5 mL/min, $\lambda = 254$ nm), $t_R = 15.433$ min (major), $t_R = 20.350$ min (minor), $[\alpha]_D^{25} = -154.872$ (CHCl_3 , $c = 0.39$ g/100mL for 97% ee); IR (neat) ν_{max} 2922, 1697, 1595, 1500, 1154 and 754 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 8.19 (2H, d, $J = 8.2$ Hz), 7.84 (2H, d, $J = 7.6$ Hz), 7.49-7.36 (5H, m), 7.25-7.21 (1H, m), 7.01-6.98 (6H, m), 6.86 (1H, br s), 6.71 (1H, quin, $J = 6.5$ Hz), 5.63 (1H, d, $J = 15.5$ Hz), 4.79-4.77 (1H, m), 4.14-4.06 (2H, m), 4.03 (1H, d, $J = 10.6$ Hz), 3.75-3.70 (1H, m), 3.68-3.59 (1H, m), 3.20 (1H, br s), 2.46 (3H, s), 2.22-2.14 (1H, m), 2.10 (3H, s), 2.07-1.96 (3H, m), 1.84-1.75 (1H, m), 1.21 (3H, t, $J = 7.1$ Hz); ^{13}C NMR (100 MHz, CDCl_3 , DEPT-135) δ 172.2 (C, O-C=O), 165.6 (C, N-C=O), 160.8 (C, C=N), 144.8 (CH), 143.7 (C), 140.4 (C), 138.8 (C), 137.6 (C), 134.8 (C), 134.5 (C), 134.1 (C), 129.5 (3CH), 128.9 (CH), 128.8, 128.8 (3CH), 128.7 (3CH), 128.3 (CH), 127.6 (CH), 127.1 (C), 127.1 (CH), 126.4 (CH), 125.3 (CH), 124.0 (CH), 119.0 (3CH), 61.2 (C), 60.4 (CH_2), 50.0 (CH_2), 49.3 (CH), 45.2 (CH), 40.4 (CH), 31.7 (CH_2), 31.0 (CH_2), 21.6 (CH_3), 14.2 (CH_3), 14.0 (CH_3); HRMS (ESI) m/z : 756.2269 $[\text{M} + \text{Na}]^+$, calcd for $\text{C}_{42}\text{H}_{40}\text{ClN}_3\text{O}_5\text{SNa}$; Found 756.2271.

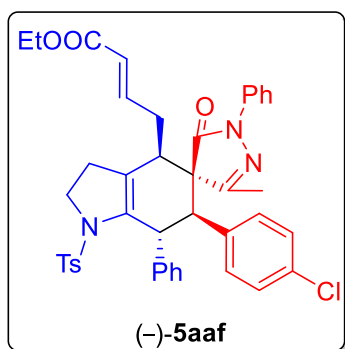
Ethyl(*E*)-4-((4*R*,5*R*,6*S*,7*S*)-6-(3-chlorophenyl)-3'-methyl-5'-oxo-1',7-diphenyl-1-tosyl-1,1',2,3,4,5',6,7-octahydrospiro[indole-5,4'-pyrazol]-4-yl)but-2-enoate (5aae):



Prepared by following general procedure **D** purified by column chromatography using EtOAc/hexane and isolated product **5aae** in 73% yield as a pale-yellow solid with M. P. 131-135 °C. The enantiomeric excess (ee) was determined by chiral stationary phase HPLC using a Daicel Chiralpak IC column (hexane/EtOAc = 70:30, flow rate 0.5 mL/min, $\lambda = 254$ nm), $t_R = 17.441$ min (major), $t_R = 22.359$ min (minor), $[\alpha]_D^{25} = -162.000$ (CHCl_3 , $c = 0.45$ g/100mL for 96% ee);

IR (neat) ν_{\max} 2924, 1699, 1654, 1597, 1492, 1159, 750 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 8.19 (2H, d, $J = 8.2$ Hz), 7.80 (2H, d, $J = 7.6$ Hz), 7.45-7.41 (2H, m), 7.39-7.37 (2H, m), 7.23 (1H, t, $J = 7.5$ Hz), 7.09-7.06 (3H, m), 6.99-6.97 (2H, m), 6.87-6.86 (3H, m), 6.68 (1H, quin, $J = 7.1$ Hz), 5.61 (1H, d, $J = 15.5$ Hz), 4.80 (1H, d, $J = 8.5$ Hz), 4.13-4.05 (2H, m), 3.72-3.67 (1H, m), 3.62-3.54 (1H, m), 3.13 (1H, br s), 3.06 (1H, d, $J = 10.5$ Hz), 2.46 (3H, s), 2.20-2.12 (1H, m), 2.04-2.00 (1H, m), 1.98 (3H, s), 1.96-1.91 (2H, m), 1.79-1.75 (1H, m), 1.20 (3H, t, $J = 7.1$ Hz); ^{13}C NMR (100 MHz, CDCl_3 , DEPT-135) δ 171.9 (C, O-C=O), 165.6 (C, N-C=O), 160.1 (C, C=N), 144.6 (CH), 143.7 (C), 140.2 (C), 140.1 (C), 137.5 (C), 135.2 (C), 134.2 (C), 133.5 (C), 129.5 (3CH), 128.9 (3CH), 128.7 (3CH), 128.5 (CH), 127.9 (3CH), 127.2 (C), 126.4 (CH), 125.4 (CH), 124.0 (CH), 119.0 (3CH), 61.2 (C), 60.4 (CH_2), 55.5 (CH), 50.0 (CH_2), 44.5 (CH), 39.9 (CH), 31.8 (CH_2), 30.9 (CH_2), 21.6 (CH_3), 14.1 (CH_3), 14.0 (CH_3); HRMS (ESI) m/z : 756.2269 $[\text{M} + \text{Na}]^+$, calcd for $\text{C}_{42}\text{H}_{40}\text{ClN}_3\text{O}_5\text{SNa}$; Found 756.2266.

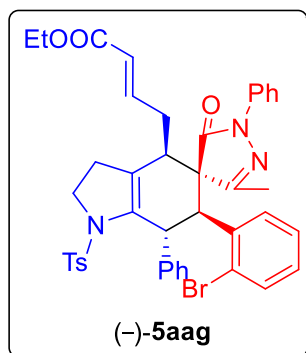
Ethyl(*E*)-4-((4*R*,5*R*,6*S*,7*S*)-6-(4-chlorophenyl)-3'-methyl-5'-oxo-1',7-diphenyl-1-tosyl-1,1',2,3,4,5',6,7-octahydrospiro[indole-5,4'-pyrazol]-4-yl)but-2-enoate (5aaf**):**



Prepared by following general procedure **D** purified by column chromatography using EtOAc/hexane and isolated product **5aaf** in 85% yield as a Off white solid with M. P. 125-127 °C. The enantiomeric excess (ee) was determined by chiral stationary phase HPLC using a Daicel Chiralpak IC column (hexane/EtOAc = 70:30, flow rate 0.5 mL/min, $\lambda = 254$ nm), $t_R = 13.219$ min (major), $t_R = 17.364$ min (minor), $[\alpha]_D^{25} = -136.923$ (CHCl_3 , $c = 1.82$ g/100mL for 96% ee); IR (neat) ν_{\max} 2924, 1701, 1654, 1597, 1492, 1157 and 750 cm^{-1} ; ^1H NMR (400 MHz,

CDCl_3) δ 8.19 (2H, d, $J = 8.2$ Hz), 7.80 (2H, d, $J = 7.6$ Hz), 7.45-7.37 (4H, m), 7.25-7.21 (1H, m), 7.1-7.03 (3H, m), 6.99-6.97 (2H, m), 6.87-6.86 (3H, m), 6.71-6.63 (1H, m), 5.61 (1H, d, $J = 15.4$ Hz), 4.81-4.78 (1H, m), 4.14-4.03 (2H, m), 3.72-3.53 (2H, m), 3.14 (1H, br s), 3.07 (1H, d, $J = 10.5$ Hz), 2.46 (3H, s), 2.19-2.12 (1H, m), 2.03-1.99 (1H, m), 1.97 (3H, s), 1.95-1.9 (1H, m), 1.74-1.65 (2H, m), 1.19 (3H, t, $J = 7$ Hz); ^{13}C NMR (100 MHz, CDCl_3 , DEPT-135) δ 171.9 (C, O-C=O), 165.6 (C, N-C=O), 160.2 (C, C=N), 144.6 (CH), 143.8 (C), 140.2 (C), 140.1 (C), 137.5 (C), 135.2, (C) 134.3 (C), 133.5 (C), 129.5 (2CH), 128.9 (3CH), 128.9 (CH), 128.8 (3CH), 128.5 (CH), 127.9 (2CH), 127.3 (C), 126.4 (CH), 125.4 (CH), 124.0 (CH), 119.0 (3CH), 61.2 (C), 60.4 (CH_2), 55.5 (CH), 50.0 (CH_2), 44.6 (CH), 39.9 (CH), 31.9 (CH_2), 30.9 (CH_2), 21.9 (CH_2), 21.6 (CH_3), 14.2 (CH_3), 14.0 (CH_3); HRMS (ESI) m/z : 756.2269 $[\text{M} + \text{Na}]^+$, calcd for $\text{C}_{42}\text{H}_{40}\text{ClN}_3\text{O}_5\text{SNa}$; Found 756.2277.

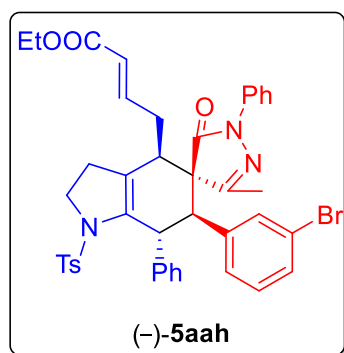
Ethyl(*E*)-4-((4*R*,5*R*,6*R*,7*S*)-6-(2-bromophenyl)-3'-methyl-5'-oxo-1',7-diphenyl-1-tosyl-1,1',2,3,4,5',6,7-octahydrospiro[indole-5,4'-pyrazol]-4-yl)but-2-enoate (5aag**):**



Prepared by following general procedure **D** purified by column chromatography using EtOAc/hexane and isolated product **5aag** in 74% yield as a pale-yellow solid with M. P. 133-135 °C. The enantiomeric excess (ee) was determined by chiral stationary phase HPLC using a Daicel Chiralpak IC column (hexane/EtOAc = 70:30, flow rate 0.5 mL/min, λ = 254 nm), t_R = 13.219 min (major), t_R = 17.364 min (minor), $[\alpha]_D^{25}$ = -121.347 (CHCl₃, c = 1.93 g/100mL for 96% ee); IR (neat) ν_{\max} 2939, 1716, 1691, 1597, 1498, 1159 and 750 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 8.19

(2H, d, J = 8.2 Hz), 7.84 (2H, d, J = 7.6 Hz), 7.48-7.41 (3H, m), 7.37 (2H, d, J = 8.1 Hz), 7.25-7.21 (2H, m), 7.08-7.02 (4H, m), 6.98-6.89 (2H, m), 6.71 (1H, quin, J = 6.9 Hz), 5.62 (1H, d, J = 15.5 Hz), 4.79-4.76 (1H, m), 4.15-4.03 (2H, m), 3.99 (1H, d, J = 10.5 Hz), 3.75-3.60 (2H, m), 3.24 (1H, br s), 2.45 (3H, s), 2.21-2.15 (1H, m), 2.14 (3H, s), 2.04-1.97 (2H, m), 1.85-1.79 (1H, m), 1.68 (1H, br s), 1.2 (3H, t, J = 7.1 Hz); ¹³C NMR (100 MHz, CDCl₃, DEPT-135) δ 172.2 (C, O-C=O), 165.6 (C, N-C=O), 160.9 (C, C=N), 144.8 (CH), 143.7 (C), 140.3 (C), 138.6 (C), 137.6 (C), 136.5 (C), 134.5 (C), 133.0 (CH), 129.5 (3CH), 129.2 (CH), 128.9 (3CH), 128.7 (3CH), 128.5 (CH), 127.7 (CH), 127.6 (C), 127.1 (C), 126.5 (CH), 125.3 (CH), 124.0 (CH), 119.0 (3CH), 61.3 (C), 60.4 (CH₂), 52.0 (CH), 50.0 (CH₂), 45.5 (CH), 40.4 (CH), 31.7 (CH₂), 31.0 (CH₂), 21.7 (CH₃), 14.5 (CH₃), 14.2 (CH₃); HRMS (ESI) m/z : 800.1764 [M + Na]⁺, calcd for C₄₂H₄₀BrN₃O₅SNa; Found 800.1768.

Ethyl(*E*)-4-((4*R*,5*R*,6*S*,7*S*)-6-(3-bromophenyl)-3'-methyl-5'-oxo-1',7-diphenyl-1-tosyl-1,1',2,3,4,5',6,7-octahydrospiro[indole-5,4'-pyrazol]-4-yl)but-2-enoate (5aah**):**

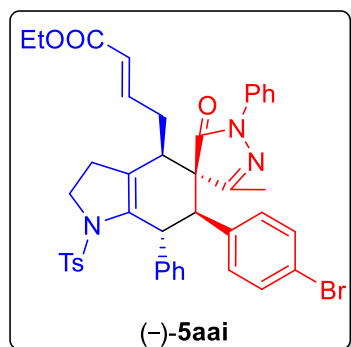


Prepared by following general procedure **D** purified by column chromatography using EtOAc/hexane and isolated product **5aah** in 67% yield as a white solid with M. P. 158-162 °C. The enantiomeric excess (ee) was determined by chiral stationary phase HPLC using a Daicel Chiralpak IC column (hexane/EtOAc = 70:30, flow rate 0.5 mL/min, λ = 254 nm), t_R = 17.2019 min (major), t_R = 22.355 min (minor), $[\alpha]_D^{25}$ = -126.098 (CHCl₃, c = 0.82 g/100mL for 95% ee); IR (neat) ν_{\max} 2918, 1720 (C=O), 1693, 1597, 1498 and 682 cm⁻¹; ¹H NMR (400 MHz,

CDCl₃) δ 8.19 (2H, d, J = 8.1 Hz), 7.80 (2H, d, J = 8 Hz), 7.45-7.36 (4H, m), 7.25-7.17 (2H, m), 7.11-7.08 (3H, m), 6.89-6.87 (4H, m), 6.68 (1H, quin, J = 7.4 Hz), 5.62 (1H, d, J = 15.5 Hz), 4.81 (1H, d, J = 10.3 Hz), 4.15-4.04 (2H, m), 3.73-3.68 (1H, m), 3.63-3.55 (1H, m), 3.13 (1H, br s), 3.03 (1H, d, J = 10.5 Hz), 2.45 (3H, s), 2.17 (1H, quin, J = 7.3 Hz), 2.04-2.02 (1H, m), 1.99 (3H, s), 1.97-1.91 (1H, m), 1.83-1.61 (2H, m), 1.20 (3H, t, J = 7 Hz); ¹³C NMR (100 MHz, CDCl₃, DEPT-135) δ 171.8 (C, O-C=O), 165.6 (C, N-C=O), 160.1 (C, C=N), 144.6 (2CH), 143.7 (C), 140.2 (2C), 140.0 (C), 138.9 (C), 137.4 (C), 134.3 (C), 130.9 (CH), 129.8 (CH), 129.5 (3CH), 128.9 (3CH), 128.8 (3CH), 127.9 (2CH), 127.3 (C), 126.5 (CH), 125.5 (CH), 124.1 (2CH), 119.3 (CH), 61.2 (C), 60.4 (CH₂), 55.8 (CH), 50.0 (CH₂), 44.4 (CH),

39.8 (CH), 31.9 (CH₂), 30.9 (CH₂), 21.6 (CH₃), 14.2 (CH₃), 14.0 (CH₃); HRMS (ESI) *m/z*: 800.1764 [M + Na]⁺, calcd for C₄₂H₄₀BrN₃O₅SNa; Found 800.1768.

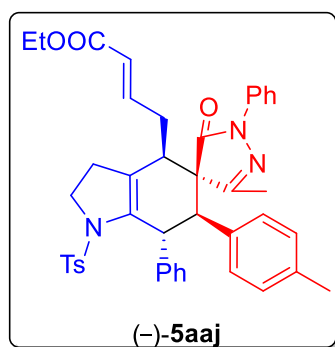
Ethyl(*E*)-4-((4*R*,5*R*,6*S*,7*S*)-6-(4-bromophenyl)-3'-methyl-5'-oxo-1',7-diphenyl-1-tosyl-1,1',2,3,4,5',6,7-octahydrospiro[indole-5,4'-pyrazol]-4-yl)but-2-enoate (5aai**):**



Prepared by following general procedure **D** purified by column chromatography using EtOAc/hexane and isolated product **5aai** in 82% yield as a white solid with M. P. 155-158 °C. The enantiomeric excess (ee) was determined by chiral stationary phase HPLC using a Daicel Chiralpak IC column (hexane/EtOAc = 70:30, flow rate 0.5 mL/min, λ = 254 nm), *t_R* = 13.276 min (major), *t_R* = 17.445 min (minor), [α]_D²⁵ = -166.800 (CHCl₃, *c* = 0.25 g/100mL for 96% ee); IR (neat) *ν*_{max} 2922, 1699, 1653, 1597, 1490, 1159 and 648 cm⁻¹; ¹H NMR (400 MHz, CDCl₃)

δ 8.19 (2H, md, *J* = 8.4Hz), 7.80 (2H, d, *J* = 7.6 Hz), 7.44 (2H, t, *J* = 7.2 Hz), 7.38 (2H, d, *J* = 8 Hz), 7.24 (1H, t, *J* = 7.2 Hz), 7.14-7.06 (5H, m), 6.87 (3H, d, *J* = 6Hz), 6.68 (1H, quin, *J* = 6.8 Hz), 5.61 (1H, d, *J* = 15.6 Hz), 4.80 (1H, d, *J* = 10.8 Hz), 4.15-4.03 (2H, m), 3.73-3.54 (2H, m), 3.14 (1H, br s), 3.05 (1H, d, *J* = 10.4 Hz), 2.46 (3H, s), 2.16 (1H, quin, *J* = 8 Hz), 2.04-2.00 (1H, m), 1.98 (3H, s), 1.97-1.91 (1H, m), 1.79-1.69 (1H, br m), 1.64 (1H, br s), 1.20 (3H, t, *J* = 7.2 Hz); ¹³C NMR (100 MHz, CDCl₃, DEPT-135) δ 171.9 (C, O-C=O), 165.6 (C, N-C=O), 160.1 (C, C=N), 144.6 (2CH), 143.7 (C), 140.3 (C), 140.1 (C), 137.5 (C), 135.8 (C), 134.3 (C), 131.4 (CH), 129.5 (3CH), 128.9 (3CH), 128.8 (3CH), 127.9 (2CH), 127.2 (C), 126.4 (CH), 125.4 (CH), 124.1 (CH), 121.7 (C), 119.1 (3CH), 61.2 (C), 60.4 (CH₂), 55.6 (CH), 50.0 (CH₂), 44.5 (CH), 40.0 (CH), 31.9 (CH₂), 30.9 (CH₂), 21.7 (CH₃), 14.2 (CH₃), 14.0 (CH₃); HRMS (ESI) *m/z*: 800.1764 [M + Na]⁺, calcd for C₄₂H₄₀BrN₃O₅SNa; Found 800.1766.

Ethyl(*E*)-4-((4*R*,5*R*,6*S*,7*S*)-3'-methyl-5'-oxo-1',7-diphenyl-6-(*p*-tolyl)-1-tosyl-1,1',2,3,4,5',6,7-octahydrospiro[indole-5,4'-pyrazol]-4-yl)but-2-enoate (5aaj**):**



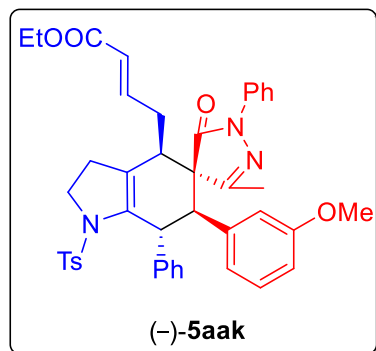
Prepared by following general procedure **D** purified by column chromatography using EtOAc/hexane and isolated product **5aaj** in 80% yield as a pale-yellow solid with M. P. 205-208 °C. The enantiomeric excess (ee) was determined by chiral stationary phase HPLC using a Daicel Chiralpak IC column (hexane/EtOAc = 70:30, flow rate 0.5 mL/min, λ = 254 nm), *t_R* = 16.070 min (major), *t_R* = 21.051 min (minor), [α]_D²⁵ = -170.000 (CHCl₃, *c* = 0.14g/100mL for 97% ee); IR (neat) *ν*_{max}

2918, 1718, 1697, 1597, 1454, 1157 and 760 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 8.21 (2H, d, *J* = 8.2Hz), 7.81 (2H, d, *J* = 7.6Hz), 7.44-7.40 (2H, m), 7.38-7.36 (2H, m), 7.24-7.20 (1H, m), 7.09-7.04 (3H, m), 6.88-6.78 (5H, m), 6.69 (1H, quin, *J* = 7 Hz), 5.61 (1H, d, *J* = 15.4 Hz), 4.82-4.8 (1H, m), 4.13-4.05 (2H, m), 3.72-3.54 (2H, m), 3.12 (1H, br s), 3.03 (1H, d, *J* = 10.52 Hz), 2.45 (3H, s), 2.2-2.15 (1H, m), 2.14 (3H, s), 1.99 (3H, s), 1.97-1.90 (2H, m), 1.78-1.69 (2H, m), 1.21 (3H, t, *J* = 7.1Hz); ¹³C NMR (100 MHz, CDCl₃, DEPT-135) δ 172.1 (C, O-C=O), 165.7 (C, N-C=O), 160.5 (C, C=N), 144.9 (2CH), 143.6 (C), 140.6 (C), 137.7 (C), 137.2 (C), 134.4 (C), 133.3 (C), 132.2 (C), 132.1 (C), 129.4 (3CH), 129.0 (CH),

128.8 (5CH), 127.7 (2CH), 126.1 (CH), 125.2 (2CH), 123.9 (CH), 119.2 (3CH), 61.5 (C), 60.4 (CH₂), 55.8 (CH), 50.0 (CH₂), 44.6 (CH), 40.0 (CH), 31.9 (CH₂), 31.0 (CH₂), 21.7 (CH₃), 21.0 (CH₃), 14.2 (CH₃), 14.0 (CH₃); HRMS (ESI) *m/z*: 736.2816 [M + Na]⁺, calcd for C₄₃H₄₃N₃O₅SNa; Found 736.2842.

Ethyl(*E*)-4-((4*R*,5*R*,6*S*,7*S*)-6-(3-methoxyphenyl)-3'-methyl-5'-oxo-1',7-diphenyl-1-tosyl-1,1',2,3,4,5',6,7-octahydrospiro[indole-5,4'-pyrazol]-4-yl)but-2-enoate (5aak**):**

Prepared by following general procedure **D** purified by column chromatography using EtOAc/hexane

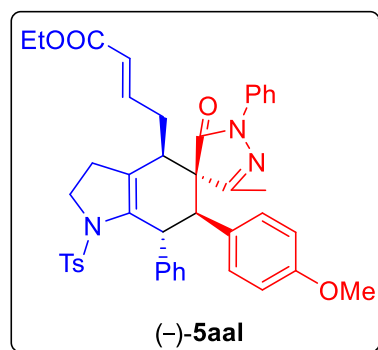


and isolated product **5aak** in 66% yield as a off white solid with M. P.

113-115 °C. The enantiomeric excess (ee) was determined by chiral stationary phase HPLC using a Daicel Chiralpak IC column (hexane/EtOAc = 70:30, flow rate 0.5 mL/min, λ = 254 nm), *t_R* = 14.328 min (major), *t_R* = 20.170 min (minor), [α]_D²⁵ = **-117.931** (CHCl₃, c = 1.74 g/100mL for 96% ee); IR (neat) ν_{max} 2976, 1697,

1595, 1490, 1292, 1157 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 8.21 (2H, d, *J* = 8.2 Hz), 7.83 (2H, d, *J* = 7.6 Hz), 7.43-7.37 (4H, m), 7.21 (1H, t, *J* = 7.4 Hz), 7.09-7.02 (3H, m), 6.88 (3H, d, *J* = 6 Hz), 6.69 (1H, quin, *J* = 7 Hz), 6.6-6.57 (1H, m), 6.44 (1H, br s), 5.61 (1H, d, *J* = 15.5 Hz), 4.85-4.82 (1H, m), 4.13-4.04 (2H, m), 3.72-3.54 (2H, m), 3.42 (3H, s), 3.13 (1H, br s), 3.05 (1H, d, *J* = 10.5 Hz), 2.46 (3H, s), 2.2-2.12 (1H, m), 2.04-2.0 (1H, m), 1.99 (3H, s), 1.94-1.90 (1H, m), 1.83-1.66 (2H, m), 1.20 (3H, t, *J* = 7.1 Hz); ¹³C NMR (100 MHz, CDCl₃, DEPT-135) δ 172.1 (C, O-C=O), 165.7 (C, N-C=O), 160.5 (C, C=N), 144.9 (2CH), 143.6 (C), 140.6 (C), 140.5 (C), 137.7 (C), 137.2 (C), 134.4 (C), 133.3 (C), 132.2 (C), 132.1 (C), 129.4 (3C), 128.8 (CH), 128.8 (4CH) 127.8 (3CH), 126.1 (CH), 125.2 (CH), 123.9 (CH), 119.2 (3CH), 61.5 (C), 60.4 (CH₂), 56.2 (CH), 55.0 (CH₃) 50.0 (CH₂), 44.5 (CH), 40.1 (CH), 31.9 (CH₂), 30.9 (CH₂), 21.7 (CH₃), 14.2 (CH₃), 14.0 (CH₃); HRMS (ESI) *m/z*: 752.2765 [M + Na]⁺, calcd for C₄₃H₄₃N₃O₆SNa; Found 752.2766.

Ethyl(*E*)-4-((4*R*,5*R*,6*S*,7*S*)-6-(4-methoxyphenyl)-3'-methyl-5'-oxo-1',7-diphenyl-1-tosyl-1,1',2,3,4,5',6,7-octahydrospiro[indole-5,4'-pyrazol]-4-yl)but-2-enoate (5aal**):**



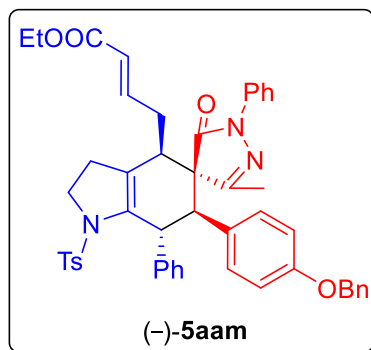
Prepared by following general procedure **D** purified by column chromatography using EtOAc/hexane and isolated product **5aal** in

84% yield as a off white solid with M. P. 113-115 °C. The enantiomeric excess (ee) was determined by chiral stationary phase HPLC using a Daicel Chiralpak IC column (hexane/EtOAc = 70:30, flow rate 0.5 mL/min, λ = 254 nm), *t_R* = 15.990 min (major), *t_R* = 22.096 min (minor), [α]_D²⁵ = **-123.662** (CHCl₃, c = 1.42 g/100mL for 96% ee); IR (neat) ν_{max} 2918, 1699, 1597, 1512,

1492, 1159 and 754 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 8.20 (2H, d, *J* = 8.2 Hz), 7.81 (2H, d, *J* = 7.6 Hz), 7.44-7.36 (5H, m), 7.24-7.20 (1H, m), 7.08-7.05 (3H, m), 6.88-6.86 (2H, m), 6.7 (1H, quin, *J* = 7 Hz), 6.53-6.51 (2H, m), 5.62 (1H, d, *J* = 15.4 Hz), 4.81-4.79 (1H, m), 4.13-4.05 (2H, m), 3.73-3.68 (2H, m), 3.64 (3H, s), 3.61-3.57 (1H, m), 3.12 (1H, br s), 3.02 (1H, d, *J* = 10.5 Hz), 2.46 (3H, s), 2.41-2.36 (1H, m), 2.20-2.12 (2H, m), 1.99 (3H, s), 1.96-1.91 (1H, m), 1.21 (3H, t, *J* = 7.1 Hz); ¹³C NMR (100 MHz,

CDCl₃, DEPT-135) δ 172.2 (C, O-C=O), 165.7 (C, N-C=O), 160.5 (C, C=N), 158.8 (C), 144.9 (2CH), 143.6 (C), 140.6 (C), 140.5 (C), 137.7 (C), 134.4 (C), 129.4 (3CH), 128.8 (CH), 128.8 (4CH), 128.5 (C), 128.4 (C), 127.7 (3CH), 126.2 (CH), 125.2 (CH), 123.9 (CH), 119.1 (3CH), 113.6 (CH), 61.5 (C), 60.4 (CH₂), 55.4 (CH), 55.0 (CH₃), 50.0 (CH₂), 44.7 (CH), 40.0 (CH), 31.9 (CH₂), 31.0 (CH₂), 21.6 (CH₃), 14.2 (CH₃), 14.0 (CH₃); HRMS (ESI) m/z : 752.2765 [M + Na]⁺, calcd for C₄₃H₄₃N₃O₆SNa; Found 752.2762.

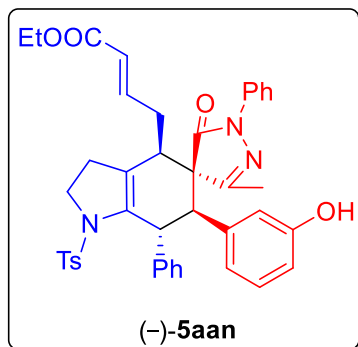
Ethyl(*E*)-4-((4*R*,5*R*,6*S*,7*S*)-6-(4-(benzyloxy)phenyl)-3'-methyl-5'-oxo-1',7-diphenyl-1-tosyl-1,1',2,3,4,5',6,7-octahydrospiro[indole-5,4'-pyrazol]-4-yl)but-2-enoate (5aam):



Prepared by following general procedure **D** purified by column chromatography using EtOAc/hexane and isolated product **5aam** in 73% yield as a pale-yellow solid with M. P. 112-114 °C. The enantiomeric excess (ee) was determined by chiral stationary phase HPLC using a Daicel Chiralpak IC column (hexane/EtOAc = 70:30, flow rate 0.5 mL/min, λ = 254 nm), t_R = 14.691 min (major), t_R = 19.857 min (minor), $[\alpha]_D^{25}$ = -129.793 (CHCl₃, c = 1.45 g/100mL for 94% ee); IR (neat) ν_{\max} 2920, 1697, 1595, 1510, 1454, 1290 and

754 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 8.2 (2H, d, J = 8.2 Hz), 7.8 (2H, d, J = 7.5 Hz), 7.43-7.36 (4H, m), 7.34-7.31 (4H, m), 7.3-7.27 (1H, m), 7.21 (1H, t, J = 7.4 Hz), 7.1-7.05 (3H, m), 6.88-6.86 (3H, m), 6.69 (1H, quin, J = 7 Hz), 6.61-6.59 (2H, m), 5.61 (1H, d, J = 15.5 Hz), 4.89-4.79 (3H, m), 4.15-4.03 (2H, m), 3.72-3.54 (2H, m), 3.13 (1H, br s), 3.03 (1H, d, J = 10.5 Hz), 2.45 (3H, s), 2.2-2.12 (1H, m), 2.05-2.0 (1H, m), 1.99 (3H, s), 1.94-1.90 (1H, m), 1.79-1.66 (2H, m), 1.2 (3H, t, J = 7.1 Hz); ¹³C NMR (100 MHz, CDCl₃, DEPT-135) δ 172.2 (C, O-C=O), 165.7 (C, N-C=O), 160.5 (C, C=N), 158.1 (C), 144.9 (CH), 143.6 (C), 140.6 (C), 140.5 (2C), 137.7 (C), 136.7 (C), 134.4 (C), 129.5 (2CH), 128.8 (3CH), 128.8 (3CH), 128.5 (3CH), 128.0 (CH), 127.8 (2CH), 127.6 (3CH), 127.1 (C), 126.2 (CH), 125.2 (CH), 123.9 (CH), 119.2 (3CH), 114.5 (CH), 69.8 (CH₂), 61.5 (C), 60.4 (CH₂), 55.4 (CH), 50.0 (CH₂), 44.8 (CH), 40.0 (CH), 32.0 (CH₂), 30.9 (CH₂), 21.6 (CH₃), 14.2 (CH₃), 14.0 (CH₃); HRMS (ESI) m/z : 828.3078 [M + Na]⁺, calcd for C₄₉H₄₇N₃O₆SNa; Found 828.3077.

Ethyl(*E*)-4-((4*R*,5*R*,6*S*,7*S*)-6-(3-hydroxyphenyl)-3'-methyl-5'-oxo-1',7-diphenyl-1-tosyl-1,1',2,3,4,5',6,7-octahydrospiro[indole-5,4'-pyrazol]-4-yl)but-2-enoate (5aan):

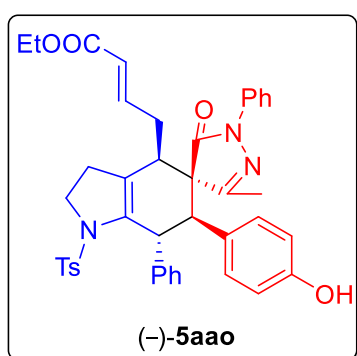


Prepared by following general procedure **D** purified by column chromatography using EtOAc/hexane and isolated product **5aan** in 41% yield as a pale-yellow solid with M. P. 120-122 °C. The enantiomeric excess (ee) was determined by chiral stationary phase HPLC using a Daicel Chiralpak IC column (hexane/EtOAc = 70:30, flow rate 0.5 mL/min, λ = 254 nm), t_R = 13.444 min (major), t_R = 16.238 min (minor), $[\alpha]_D^{25}$ = -103.314 (CHCl₃, c = 0.5 g/100mL for 93% ee); IR (neat) ν_{\max} 3404, 2924, 1697, 1597, 1456 and 1157 cm⁻¹; ¹H NMR

(400 MHz, CDCl₃) δ 8.18 (2H, d, J = 8.2 Hz), 7.78 (d, 2H, J = 7.7 Hz), 7.44-7.36 (m, 4H), 7.24-7.20 (m,

1H), 7.1-7.03 (m, 4H), 6.93-6.84 (m, 3H), 6.7 (1H, quin, $J = 7.1$ Hz), 6.54-6.52 (1H, m), 6.41 (1H, broad), 5.63 (1H, d, $J = 15.5$ Hz), 4.82-4.8 (1H, m), 4.14-4.06 (2H, m), 3.73-3.54 (2H, m), 3.13 (1H, broad), 3.02 (1H, d, $J = 10.5$ Hz), 2.46 (3H, s), 2.21-2.13 (1H, m), 2.04-2.03 (1H, m), 2.0 (3H, s), 1.94-1.92 (1H, m), 1.82-1.76 (2H, m), 1.21 (3H, t, $J = 7$ Hz); ^{13}C NMR (100 MHz, CDCl_3 , DEPT-135) δ 172.2 (C, C-C=O), 165.8 (C, N-C=O), 160.5 (C, C=N), 144.9 (CH), 143.7 (C), 140.4 (C), 140.3 (C), 138.1 (C), 137.6 (C), 134.4 (C), 132.1 (CH), 132.0 (CH), 129.5 (3CH), 129.4 (C), 128.8 (3CH), 128.7 (2CH), 128.7 (CH), 128.5 (CH), 127.8 (2CH), 127.1 (C), 126.3 (CH), 125.4 (CH), 123.9 (CH), 119.4 (CH), 114.8 (CH), 61.4, (C) 60.5 (CH_2), 55.9 (CH), 50.0 (CH_2), 44.5 (CH), 39.9 (CH), 31.9 (CH_2), 30.9 (CH_2), 21.6 (CH_3), 14.2 (CH_3), 14.0 (CH_3); HRMS (ESI) m/z : 738.2608 $[\text{M} + \text{Na}]^+$, calcd for $\text{C}_{42}\text{H}_{41}\text{N}_3\text{O}_6\text{SNa}$; Found 738.2609.

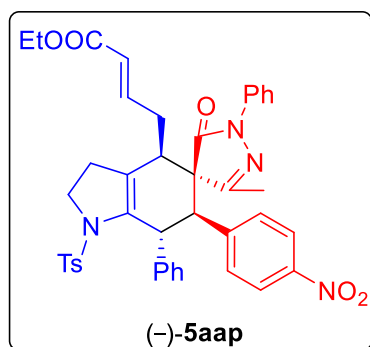
Ethyl(*E*)-4-((4*R*,5*R*,6*S*,7*S*)-6-(4-hydroxyphenyl)-3'-methyl-5'-oxo-1',7-diphenyl-1-tosyl-1,1',2,3,4,5',6,7-octahydrospiro[indole-5,4'-pyrazol]-4-yl)but-2-enoate (5aao):



Prepared by following general procedure **D** purified by column chromatography using EtOAc/hexane and isolated product **5aao** in 53% yield as a pale-yellow solid with M. P. 96-98 °C. The enantiomeric excess (ee) was determined by chiral stationary phase HPLC using a Daicel Chiralpak IC column (hexane/EtOAc = 70:30, flow rate 0.5 mL/min, $\lambda = 254$ nm), $t_R = 15.820$ min (major), $t_R = 22.353$ min (minor), $[\alpha]_D^{25} = -83.898$ (CHCl_3 , $c = 0.12$ g/100mL for 74% ee); IR (neat) ν_{max} 3456, 2922, 1699, 1597, 1438, 1516 and 758.02 cm^{-1} ; ^1H NMR

(400 MHz, CDCl_3) δ 8.19 (2H, d, $J = 8.2$ Hz), 7.81 (2H, d, $J = 7.6$ Hz), 7.44-7.36 (4H, m), 7.24-7.19 (1H, m), 7.1-7.05 (3H, m), 6.88-6.86 (3H, m), 6.73-6.65 (2H, m), 6.47-6.45 (2H, m), 5.61 (1H, d, $J = 15.5$ Hz), 4.8-4.77 (1H, m), 4.13-4.05 (2H, m), 3.73-3.55 (2H, m), 3.12 (1H, br s), 3.01 (1H, d, $J = 10.5$ Hz), 2.46 (3H, s), 2.2-2.12 (1H, m), 2.04-2.01 (1H, m), 1.99 (3H, s), 1.95-1.91 (1H, m), 1.83-1.74 (2H, m), 1.21 (3H, t, $J = 7.1$ Hz); ^{13}C NMR (100 MHz, CDCl_3 , DEPT-135) δ 172.2 (C, O-C=O), 165.7 (C, N-C=O), 160.5 (C, C=N), 155.23 (C), 144.9 (CH), 143.6 (C), 137.7 (C), 134.4 (C), 132.2 (2CH), 132.1 (3CH), 129.4 (2CH), 128.8 (2CH), 128.8 (2CH), 128.6 (2CH), 128.5 (2CH), 127.7 (2CH), 127.0 (C), 126.2 (CH), 125.2 (CH), 123.9 (CH), 119.1 (2CH), 61.6 (C), 60.4 (CH_2), 55.4 (CH), 50.0 (CH_2), 44.7 (CH), 40.0 (CH), 31.9 (CH_2), 29.8.9 (CH_2), 21.6 (CH_3), 14.2 (CH_3), 14.0 (CH_3); HRMS (ESI) m/z : 738.2608 $[\text{M} + \text{Na}]^+$, calcd for $\text{C}_{42}\text{H}_{41}\text{N}_3\text{O}_6\text{SNa}$; Found 738.2609.

Ethyl(*E*)-4-((4*R*,5*R*,6*S*,7*S*)-3'-methyl-6-(4-nitrophenyl)-5'-oxo-1',7-diphenyl-1-tosyl-1,1',2,3,4,5',6,7-octahydrospiro[indole-5,4'-pyrazol]-4-yl)but-2-enoate (5aap):

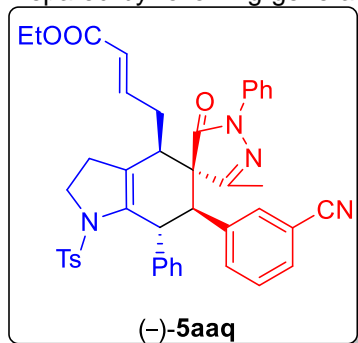


Prepared by following general procedure **D** purified by column chromatography using EtOAc/hexane and isolated product **5aap** in 62% yield as a pale-yellow solid with M. P. 85-87 °C. The enantiomeric excess (ee) was determined by chiral stationary phase HPLC using a Daicel Chiralpak IC column (hexane/EtOAc = 70:30, flow rate 0.5 mL/min, $\lambda = 254$ nm), $t_R = 21.012$ min (major), $t_R = 28.984$ min (minor), $[\alpha]_D^{25} = -126.998$ (CHCl_3 , $c = 0.46$ g/100mL for

94% ee); IR (neat) ν_{\max} 2920, 1701, 1697, 1519, 1597, 1346, 1519, 1157 and 756 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 8.19 (2H, d, $J = 8.1$ Hz), 7.87 (2H, d, $J = 8.4$ Hz), 7.79 (2H, d, $J = 8.2$ Hz), 7.45-7.38 (4H, m), 7.24-7.22 (1H, m), 7.07-7.06 (4H, m), 6.86 (2H, broad), 6.66 (1H, quin, $J = 7.5$ Hz), 5.61 (1H, d, $J = 15.4$ Hz), 4.88-4.85 (1H, m), 4.14-4.02 (2H, m), 3.73-3.54 (2H, m), 3.25 (1H, d, $J = 10.5$ Hz), 3.18 (1H, br s), 2.46 (3H, s), 2.22-2.14 (1H, m), 2.05-2.02 (1H, m), 1.98 (3H, s), 1.96-1.92 (1H, m), 1.78-1.73 (2H, m), 1.19 (3H, t, $J = 7.1$ Hz); ^{13}C NMR (100 MHz, CDCl_3 , DEPT-135) δ 171.6 (C, O-C=O), 165.5 (C, N-C=O), 159.8 (C, C=N), 147.3 (C), 144.5 (C), 144.2 (CH), 143.9 (C), 139.9 (C), 139.6 (C), 137.3 (C), 134.2 (C), 129.6 (3CH), 129.0 (3CH), 128.7 (3CH), 128.1 (2CH), 127.5 (C), 126.7 (CH), 125.6 (CH), 124.3 (CH), 123.5 (2CH), 118.9 (3CH), 61.1 (C), 60.4 (CH_2), 55.9 (CH), 50.1 (CH_2), 44.4 (CH), 39.9 (CH), 31.8 (CH_2), 30.9 (CH_2), 21.6 (CH_3), 14.2 (CH_3), 14.0 (CH_3); HRMS (ESI) m/z : 767.2510 $[\text{M} + \text{Na}]^+$, calcd for $\text{C}_{42}\text{H}_{40}\text{N}_4\text{O}_7\text{SNa}$; Found 767.2509.

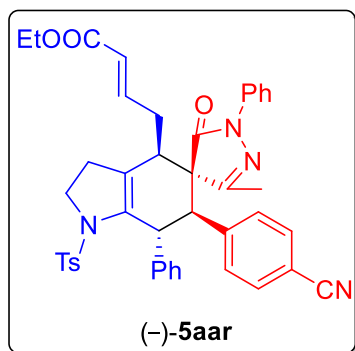
Ethyl(*E*)-4-((4*R*,5*R*,6*S*,7*S*)-6-(3-cyanophenyl)-3'-methyl-5'-oxo-1',7-diphenyl-1-tosyl-1,1',2,3,4,5',6,7-octahydrospiro[indole-5,4'-pyrazol]-4-yl)but-2-enoate (5aaq**):**

Prepared by following general procedure **D** purified by column chromatography using EtOAc/hexane



and isolated product **5aaq** in 52% yield as a yellow solid with M. P. 112-114 $^{\circ}\text{C}$. The enantiomeric excess (ee) was determined by chiral stationary phase HPLC using a Daicel Chiralpak IC column (hexane/EtOAc = 70:30, flow rate 0.5 mL/min, $\lambda = 254$ nm), $t_R = 17.161$ min (major), $t_R = 22.747$ min (minor); $[\alpha]_{\text{D}}^{25} = -114.545$ (CHCl_3 , $c = 0.11$ g/100mL for 96% ee); IR (neat) ν_{\max} 2922, 1699, 1597, 1494, 1159 and 752. cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 8.18 (2H, d, $J = 8.4$ Hz), 7.77 (2H, d, $J = 7.6$ Hz), 7.46-7.36 (6H, m), 7.24 (1H, t, $J = 7.4$ Hz), 7.16 (1H, t, $J = 7.2$ Hz), 7.09-7.08 (3H, m), 6.86-6.84 (2H, br m), 6.67 (1H, quin, $J = 7.3$ Hz), 5.62 (1H, d, $J = 15.2$ Hz), 4.82 (1H, d, $J = 10.4$ Hz), 4.15-4.03 (2H, m), 3.74 (1H, dd, $J = 4.4, 7.2$ Hz), 3.60 (1H, ddd, $J = 9.2, 9.6, 9.6$ Hz), 3.16 (1H, br s), 3.12 (1H, d, $J = 10.4$ Hz), 2.46 (3H, s), 2.19 (1H, quin, $J = 8.1$ Hz), 2.05-2.03 (1H, m), 2.01 (3H, s), 1.96-1.92 (1H, m), 1.79-1.70 (2H, m), 1.20 (3H, t, $J = 14.4$ Hz); ^{13}C NMR (100 MHz, CDCl_3 , DEPT-135) δ 171.6 (C, O-C=O), 165.5 (C, N-C=O), 159.8 (C, C=N), 144.2 (2CH), 143.8 (C), 140.0 (C), 139.6 (C), 138.4 (C), 137.2 (C), 134.2 (C), 131.6 (CH), 129.5 (3CH), 129.3 (CH), 129.0 (3CH), 128.8 (3CH), 128.1 (2CH), 127.3 (C), 126.8 (CH), 125.7 (CH), 124.3 (2CH), 119.0 (2CH), 118.2 (C, -CN), 61.1 (C), 60.5 (CH_2), 55.8 (CH), 50.0 (CH_2), 44.3 (CH), 39.8 (CH), 31.9 (CH_2), 30.9 (CH_2), 21.7 (CH_3), 14.2 (CH_3), 14.0 (CH_3); HRMS (ESI) m/z : 747.2612 $[\text{M} + \text{Na}]^+$, calcd for $\text{C}_{43}\text{H}_{40}\text{N}_4\text{O}_5\text{SNa}$; Found 722.2611.

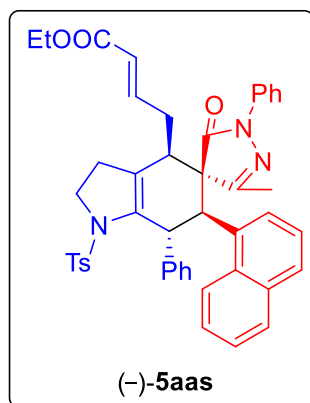
Ethyl(*E*)-4-((4*R*,5*R*,6*S*,7*S*)-6-(4-cyanophenyl)-3'-methyl-5'-oxo-1',7-diphenyl-1-tosyl-1,1',2,3,4,5',6,7-octahydrospiro[indole-5,4'-pyrazol]-4-yl)but-2-enoate (5aar**):**



Prepared by following general procedure **D** purified by column chromatography using EtOAc/hexane and isolated product **5aar** in 73% yield as a white solid with M. P. 108-110 °C. The enantiomeric excess (ee) was determined by chiral stationary phase HPLC using a Daicel Chiralpak IC column (hexane/EtOAc = 70:30, flow rate 0.5 mL/min, λ = 254 nm), t_R = 18.317 min (major), t_R = 25.259 min (minor), $[\alpha]_D^{25}$ = **-108.676 (CHCl₃, c = 1.12 g/100mL for 96% ee)**; IR (neat) ν_{\max} 2924, 2235, 1718, 1697, 1597, 1496, 1155 and 750. cm⁻¹; ¹H

NMR (400 MHz, CDCl₃) δ 8.18 (2H, d, J = 8.2 Hz), 7.78 (2H, d, J = 7.6 Hz), 7.45-7.38 (4H, m), 7.3 (2H, d, J = 8.1 Hz), 7.25 (1H, t, 7.2 Hz), 7.08-7.017 (4H, m), 6.85 (2H, br m), 6.67 (1H, quin, J = 7.3 Hz), 5.61 (1H, d, J = 15.4 Hz), 4.84 (1H, d, J = 10.4 Hz), 4.14-4.02 (2H, m), 3.71 (1H, dd, J = 7.6, 7.6 Hz), 3.59 (1H, ddd, J = 9.6, 9.6, 9.6 Hz), 3.16 (2H, br m), 2.46 (3H, s), 2.18 (1H, quin, J = 7.6 Hz), 2.05-2.01 (1H, m), 1.99 (3H, s), 1.96-1.92 (1H, m), 1.82-1.7 (2H, m), 1.19 (3H, t, J = 7.1 Hz); ¹³C NMR (100 MHz, CDCl₃, DEPT-135) δ 171.6 (C, O-C=O), 165.5 (C, N-C=O), 159.8 (C, C=N), 144.2 (2CH), 143.9 (C), 142.3 (C), 140.0 (C), 139.7 (C), 137.3 (C), 134.2 (C), 132.1 (2CH), 129.5 (2CH), 129.0 (3CH), 128.7 (2CH), 128.1 (2CH), 127.3 (C), 126.7 (CH), 125.6 (CH), 124.2 (2CH), 118.9 (3CH), 118.3 (CN), 111.8 (C), 61.1 (C), 60.4 (CH₂), 56.2 (CH), 50.0 (CH₂), 44.3 (CH), 39.9 (CH), 31.8 (CH₂), 30.9 (CH₂), 21.6 (CH₃), 14.2 (CH₃), 14.0 (CH₃); HRMS (ESI) m/z : 747.2612 [M + Na]⁺, calcd for C₄₃H₄₀N₄O₅Na; Found 722.2612.

Ethyl(*E*)-4-((4*R*,5*R*,6*S*,7*S*)-3'-methyl-6-(naphthalen-1-yl)-5'-oxo-1',7-diphenyl-1-tosyl-1,1',2,3,4,5',6,7-octahydrospiro[indole-5,4'-pyrazol]-4-yl)but-2-enoate (5aas**):**



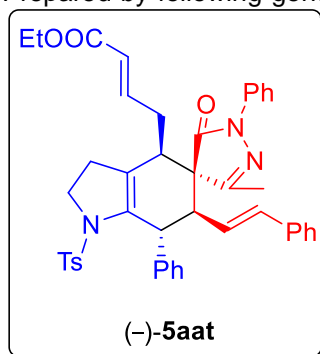
Prepared by following general procedure **D** purified by column chromatography using EtOAc/hexane and isolated product **5aas** in 61% yield as a pale-yellow solid with M. P. 131-133 °C. The enantiomeric excess (ee) was determined by chiral stationary phase HPLC using a Daicel Chiralpak IC column (hexane/EtOAc = 70:30, flow rate 0.5 mL/min, λ = 254 nm), t_R = 16.293 min (major), t_R = 24.184 min (minor), $[\alpha]_D^{25}$ = **-208.333 (CHCl₃, c = 0.18 g/100mL for 96% ee)**; IR (neat) ν_{\max} 2922, 1699, 1597, 1492, 1454, 1157 and 750. cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 8.24 (2H, d, J = 8.4 Hz), 7.83 (2H, d, J = 8 Hz), 7.64 (3H, ddd, J = 7.6,

8, 8 Hz), 7.46-7.39 (5H, m), 7.25-7.13 (4H, m), 6.94-6.80 (4H, m), 6.73 (1H, quin, J = 6.9 Hz), 5.64 (1H, d, J = 15.6 Hz), 4.99 (1H, d, J = 10.4 Hz), 4.19 (1H, d, J = 10 Hz), 4.14-4.06 (2H, m), 3.76 (1H, dd, J = 7.2, 8.7 Hz), 3.68 (1H, ddd, J = 9.2, 9.4, 9.2 Hz), 3.27 (1H, br s), 2.48 (3H, s), 2.21 (1H, quin, J = 7.2 Hz), 2.06-1.99 (2H, m), 1.91-1.81 (1H, m), 1.71 (3H, s), 1.67-1.64 (1H, m), 1.21 (3H, t, J = 7.2 Hz); ¹³C NMR (100 MHz, CDCl₃, DEPT-135) δ 172.6 (C, O-C=O), 165.7 (C, N-C=O), 160.4 (C, C=N), 145.0 (2CH), 143.7 (C), 140.8 (C), 139.8 (C), 137.7 (C), 134.5 (C), 133.4 (C), 133.4 (C), 131.5 (C), 129.5

(2CH), 128.9 (3CH), 128.8 (3CH), 128.3 (CH), 127.6 (CH), 127.0 (C), 126.2 (CH), 125.5 (CH), 125.3 (CH), 125.1 (CH), 125.0 (CH), 124.4 (CH), 123.9 (CH), 121.8 (CH), 119.1 (3CH), 61.7 (C), 60.4 (CH₂), 50.0 (CH₂), 47.8 (CH), 45.9 (CH), 40.8 (CH), 31.8 (CH₂), 31.1 (CH₂), 21.7 (CH₃), 14.2 (CH₃), 14.0 (CH₃); HRMS (ESI) *m/z*: 772.2816 [M + Na]⁺, calcd for C₄₆H₄₃N₃O₅SNa; Found 772.2811.

Ethyl(*E*)-4-((4*R*,5*S*,6*R*,7*S*)-3'-methyl-5'-oxo-1',7-diphenyl-6-((*E*)-styryl)-1-tosyl-1,1',2,3,4,5',6,7-octahydrospiro[indole-5,4'-pyrazol]-4-yl)but-2-enoate (5aat**):**

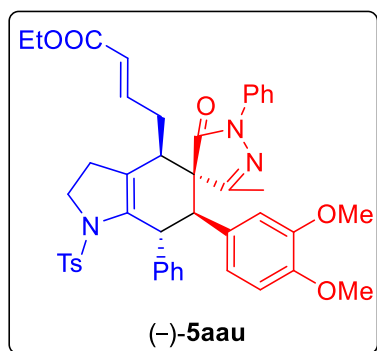
Prepared by following general procedure **D** purified by column chromatography using EtOAc/hexane and isolated product **5aat** in 68% yield as a brown solid with M. P. 95-97 °C. The enantiomeric excess (*ee*) was determined by chiral stationary phase HPLC using a Daicel Chiralpak IA column (hexane/EtOAc =



= 75:25, flow rate 0.5 mL/min, λ = 254 nm), t_R = 18.952 min (major), t_R = 22.332 min (minor), $[\alpha]_D^{25}$ = -73.600 (CHCl₃, *c* = 0.25 g/100mL for 90% *ee*); IR (neat) ν_{\max} 2924, 1701, 1597, 1496, 1288, 1157 and 748. cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 8.15 (2H, d, *J* = 8.2 Hz), 7.94 (2H, d, *J* = 7.6 Hz), 7.45 (2H, t, *J* = 7.44 Hz), 7.36 (2H, d, *J* = 7.9 Hz), 7.24-7.20 (3H,

m), 7.17-7.10 (5H, *m*), 6.99-6.96 (2H, *m*), 6.68 (1H, quin, *J* = 7.1 Hz), 5.78 (1H, d, *J* = 15.7 Hz), 5.69 (1H, dd, *J* = 9.5, 9.5 Hz), 5.61 (1H, d, *J* = 15.5 Hz), 4.52 (1H, d, *J* = 9.8 Hz), 4.15-4.03 (2H, *m*), 3.70 (1H, dd, *J* = 7.2, 8.4 Hz), 3.58 (1H, ddd, *J* = 9.3, 9.4, 9.3 Hz), 3.08 (1H, br s), 2.66 (1H, t, *J* = 9.6 Hz), 2.45 (3H, s), 2.15 (1H, quin, *J* = 7.1 Hz), 2.05 (3H, s), 2.02-1.98 (1H, *m*), 1.95-1.89 (1H, *m*), 1.76-1.67 (2H, *m*), 1.21 (3H, t, *J* = 7.1 Hz); ¹³C NMR (100 MHz, CDCl₃, DEPT-135) δ 171.8 (C, O-C=O), 165.6 (C, N-C=O), 160.8 (C, C=N), 144.7 (2CH), 143.6 (C), 140.7 (C), 139.9 (C), 137.6 (C), 136.2 (C), 135.1 (CH), 134.3 (C), 129.4 (2CH), 128.9 (2CH), 128.7 (2CH), 128.4 (3CH), 127.9 (2CH), 127.7 (CH), 127.1 (C), 126.5 (CH), 126.3 (2CH), 125.2 (CH), 124.2 (CH), 124.0 (CH), 119.0 (2CH), 60.7 (C), 60.4 (CH₂), 53.0 (CH), 50.0 (CH₂), 43.6 (CH), 39.0 (CH), 31.9 (CH₂), 30.9 (CH₂), 21.6 (CH₃), 14.2 (CH₃), 13.6 (CH₃); HRMS (ESI) *m/z*: 748.2816 [M + Na]⁺, calcd for C₄₃H₄₃N₃O₅SNa; Found 748.2816.

Ethyl(*E*)-4-((4*R*,5*R*,6*S*,7*S*)-6-(3,4-dimethoxyphenyl)-3'-methyl-5'-oxo-1',7-diphenyl-1-tosyl-1,1',2,3,4,5',6,7-octahydrospiro[indole-5,4'-pyrazol]-4-yl)but-2-enoate (5aau**):**

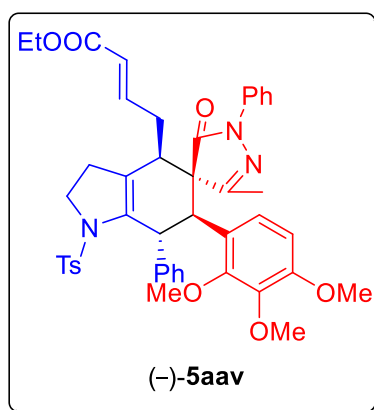


Prepared by following general procedure **D** purified by column chromatography using EtOAc/hexane and isolated product **5aau** in 72% yield as a yellow solid with M. P. 120-125 °C. The enantiomeric excess (*ee*) was determined by chiral stationary phase HPLC using a Daicel Chiralpak IC column (hexane/EtOAc = 70:30, flow rate 0.5 mL/min, λ = 254 nm), t_R = 17.759 min (major), t_R = 28.663 min (minor), $[\alpha]_D^{25}$ = -125.421 (CHCl₃, *c* = 1.66 g/100mL for 93% *ee*); IR (neat) ν_{\max} 2926, 1697, 1597, 1596, 1159 and 750. cm⁻¹; ¹H NMR

(400 MHz, CDCl₃) δ 8.21 (2H, d, *J* = 8.3 Hz), 7.86 (2H, d, *J* = 7.6 Hz), 7.42-7.37 (4H, *m*), 7.20 (1H, t, *J* = 7.4 Hz), 7.09-7.06 (3H, *m*), 6.87 (2H, d, *J* = 6.2 Hz), 6.69 (1H, quin, *J* = 8.5 Hz), 6.42 (1H, d, *J* = 7.9

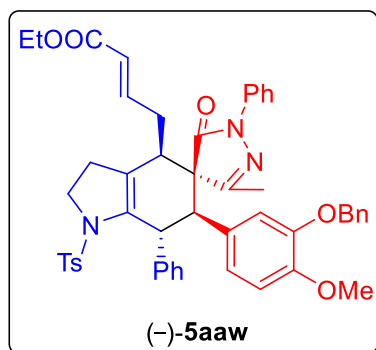
Hz), 6.18 (1H, br s), 5.61 (1H, d, $J = 15.5$ Hz), 4.79 (1H, d, $J = 10.3$ Hz), 4.14-4.02 (2H, m), 3.71 (3H, s), 3.69-3.67 (1H, m), 3.59 (1H, ddd, $J = 9.3, 9.4, 9.4$ Hz), 3.38 (3H, s), 3.13 (3H, s), 3.01 (1H, d, $J = 10.5$ Hz), 2.47 (3H, s), 2.17 (1H, quin, $J = 8.0$ Hz), 2.05-2.01 (1H, m), 1.98 (3H, s), 1.96-1.90 (1H, m), 1.78-1.67 (2H, m), 1.19 (3H, t, $J = 7.1$ Hz); ^{13}C NMR (100 MHz, CDCl_3 , DEPT-135) δ 172.4 (C, O-C=O), 165.4 (C, N-C=O), 160.6 (C, C=N), 148.7 (C), 148.2 (C), 144.8 (2CH), 143.7 (C), 140.6 (C), 140.5 (C), 137.8 (C), 134.4 (C), 129.5 (3CH), 129.0 (C), 128.9 (4CH), 128.8 (3CH), 127.8 (CH), 127.2 (C), 126.2 (CH), 125.1 (C), 124.0 (CH), 118.7 (2CH), 61.4 (C), 60.4 (CH_2), 56.0 (CH), 55.5 (CH_3), 55.5 (CH_3), 50.0 (CH_2), 44.8 (CH), 40.2 (CH), 31.9 (CH_2), 31.0 (CH_2), 21.7 (CH_3), 14.2 (CH_3), 14.0 (CH_3); HRMS (ESI) m/z : 782.2870 $[\text{M} + \text{Na}]^+$, calcd for $\text{C}_{44}\text{H}_{45}\text{N}_3\text{O}_7\text{SNa}$; Found 782.2870.

Ethyl(*E*)-4-((4*R*,5*R*,6*S*,7*S*)-3'-methyl-5'-oxo-1',7-diphenyl-1-tosyl-6-(2,3,4-trimethoxyphenyl)-1,1',2,3,4,5',6,7-octahydrospiro[indole-5,4'-pyrazol]-4-yl)but-2-enoate (5aav**):**



Prepared by following general procedure **D** purified by column chromatography using EtOAc/hexane and isolated product **5aav** in 86% yield as a white solid with M. P. 143-145 °C. The enantiomeric excess (ee) was determined by chiral stationary phase HPLC using a Daicel Chiralpak IC column (hexane/EtOAc = 70:30, flow rate 0.5 mL/min, $\lambda = 254$ nm), $t_R = 15.275$ min (major), $t_R = 21.750$ min (minor), $[\alpha]_{\text{D}}^{25} = -118.235$ (CHCl_3 , $c = 0.85$ g/100mL for 98% ee); IR (neat) ν_{max} 2927, 1718, 1693, 1597, 1498, and 1155. cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 8.21 (2H, d, $J = 8.2$ Hz), 7.80 (2H, d, $J = 7.6$ Hz), 7.42 (2H, t, $J = 7.5$ Hz), 7.37 (2H, d, $J = 8$ Hz), 7.21 (1H, t, $J = 7.4$ Hz), 7.14-7.09 (4H, m), 6.92 (1H, br s), 6.71 (1H, quin, $J = 6.9$ Hz), 6.39 (1H, d, $J = 8.8$ Hz), 5.62 (1H, d, $J = 15.5$ Hz), 4.79 (1H, d, $J = 10.5$ Hz), 4.15-4.04 (2H, m), 3.77 (1H, d, $J = 10.6$ Hz), 3.7 (3H, s), 3.69-3.68 (1H, m), 3.66 (3H, s), 3.65-3.59 (1H, m), 3.18 (1H, br s), 2.79 (3H, s), 2.45 (3H, s), 2.15 (1H, quin, $J = 7.2$ Hz), 2.04 (3H, s), 2.02-2.16 (2H, m), 1.86-1.77 (1H, m), 1.7 (1H, br s), 1.21 (3H, t, $J = 7.1$ Hz); ^{13}C NMR (100 MHz, CDCl_3 , DEPT-135) δ 172.5 (C, O-C=O), 165.7 (C, N-C=O), 161.6 (C, C=N), 152.3 (C), 151.3 (C), 145.1 (2CH), 143.6 (C), 141.4 (C), 141.0 (C), 140.4 (C), 137.8 (C), 134.6 (C), 129.5 (2CH), 128.8 (3CH), 128.7 (2CH), 127.8 (2CH), 127.1 (C), 126.2 (CH), 125.1 (CH), 123.8 (C), 122.7 (C), 122.1 (CH), 119.2 (2CH), 106.9 (CH), 61.8 (C), 60.4 (CH_3, CH_2), 60.3 (CH_3), 55.7 (CH), 49.9 (CH_2), 45.9 (CH), 44.7 (CH), 40.1 (CH), 31.8 (CH_2), 31.0 (CH_2), 21.6 (CH_3), 14.2 (CH_3), 13.4 (CH_3); HRMS (ESI) m/z : 812.2976 $[\text{M} + \text{Na}]^+$, calcd for $\text{C}_{45}\text{H}_{47}\text{N}_3\text{O}_8\text{SNa}$; Found 812.2976.

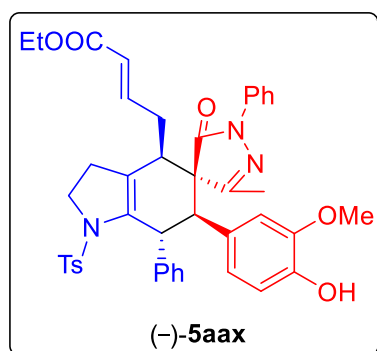
Ethyl (E)-4-((4*R*,5*R*,6*S*,7*S*)-6-(3-(benzyloxy)-4-methoxyphenyl)-3'-methyl-5'-oxo-1',7-diphenyl-1-tosyl-1,1',2,3,4,5',6,7-octahydrospiro[indole-5,4'-pyrazol]-4-yl)but-2-enoate (5aaw**):**



Prepared by following general procedure **D** purified by column chromatography using EtOAc/hexane and isolated product **5aaw** in 61% yield as a pale-yellow solid with M. P. 114-116 °C. The enantiomeric excess (ee) was determined by chiral stationary phase HPLC using a Daicel Chiralpak IC column (hexane/EtOAc = 70:30, flow rate 0.5 mL/min, λ = 254 nm), t_R = 13.895 min (major), t_R = 19.989 min (minor), $[\alpha]_D^{25}$ = **-100.385 (CHCl₃, c = 0.26 g/100mL for 85% ee)**; IR (neat) ν_{\max} 2924, 1697, 1595, 1516, 1454, 1257 and

1159. cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 8.20 (2H, d, J = 8.2 Hz), 7.90 (2H, d, J = 7.9 Hz), 7.44-7.39 (4H, m), 7.35-7.32 (2H, m), 7.28-7.26 (2H, m), 7.25 (1H, br s), 7.20 (1H, t, J = 7.4 Hz), 7.02 (3H, br s), 6.71-6.64 (4H, m), 6.43 (1H, d, J = 6.3 Hz), 5.61 (1H, d, J = 15.5 Hz), 4.63 (2H, d, J = 8.7 Hz), 4.53 (1H, d, J = 12 Hz), 4.14-4.03 (2H, m), 3.71 (3H, s), 3.69-3.66 (1H, m), 3.58 (1H, ddd, J = 9.3, 9.4, 9.3 Hz), 3.09 (1H, br s), 2.91 (1H, d, J = 10.4 Hz), 2.48 (3H, s), 2.16 (1H, quin, J = 7.6 Hz), 2.03-1.88 (5H, m), 1.78-1.62 (2H, m), 1.19 (3H, t, J = 7.1 Hz); ¹³C NMR (100 MHz, CDCl₃, DEPT-135) δ 172.4 (C, O-C=O), 165.4 (C, N-C=O), 160.4 (C, C=N), 148.8 (C), 147.6 (C), 144.8 (2CH), 143.6 (C), 140.5 (C), 140.4 (C), 137.9 (C), 136.8 (C), 134.4 (C), 129.5 (3CH), 128.9 (3CH), 128.8 (3CH), 128.7 (C), 128.6 (4CH), 127.9 (CH), 127.6 (2CH), 127.5 (CH), 127.1 (C), 126.1 (CH), 125.2 (CH), 123.9 (CH), 118.8 (2CH), 70.4 (CH₂), 61.5 (C), 60.4 (CH₂), 55.8 (CH), 55.6 (CH₃), 50.0 (C), 44.6 (CH), 40.1 (CH), 31.9 (C), 30.9 (C), 21.7 (CH₃), 14.2 (CH₃), 13.8 (CH₃); HRMS (ESI) m/z : 858.3183 [M + Na]⁺, calcd for C₅₀H₄₉N₃O₇SNa; Found 858.3184.

Ethyl(E)-4-((4*R*,5*R*,6*S*,7*S*)-6-(4-hydroxy-3-methoxyphenyl)-3'-methyl-5'-oxo-1',7-diphenyl-1-tosyl-1,1',2,3,4,5',6,7-octahydrospiro[indole-5,4'-pyrazol]-4-yl)but-2-enoate (5aax**):**



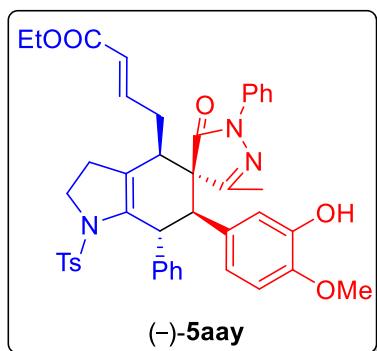
Prepared by following general procedure **D** purified by column chromatography using EtOAc/hexane and isolated product **5aax** in 81% yield as a pale-yellow solid with M. P. 93-95 °C. The enantiomeric excess (ee) was determined by chiral stationary phase HPLC using a Daicel Chiralpak IC column (hexane/EtOAc = 70:30, flow rate 0.5 mL/min, λ = 254 nm), t_R = 17.520 min (major), t_R = 25.147 min (minor), $[\alpha]_D^{25}$ = **-77.647 (CHCl₃, c = 0.5 g/100mL for 96% ee)**; IR (neat) ν_{\max} 3410, 2926, 1697, 1597,

1516, 1436 and 1290. cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 8.20 (2H, d, J = 8.2 Hz), 7.87 (2H, d, J = 7.6 Hz), 7.43-7.37 (4H, m), 7.21 (1H, t, J = 7.4 Hz), 7.10-7.05 (3H, m), 6.87 (2H, d, J = 6.3 Hz), 6.69 (1H, quin, J = 6.8 Hz), 6.48 (1H, d, J = 7.9 Hz), 6.1 (1H, br s), 5.62 (1H, d, J = 15.5 Hz), 5.42 (1H, br s), 4.77 (1H, d, J = 10.4 Hz), 4.15-4.03 (2H, m), 3.72 (1H, dd, J = 7.1, 7.1 Hz), 3.59 (1H, ddd, J = 9.2, 9.2, 9.4 Hz), 3.36 (3H, s), 3.12 (1H, br s), 2.99 (1H, d, J = 10.5 Hz), 2.47 (3H, s), 2.18 (1H, quin, J = 7.2 Hz), 2.07-2.01 (1H, m), 1.98 (3H, s), 1.96-1.91 (1H, m), 1.81-1.1 (2H, m), 1.20 (3H, t, J = 7.1 Hz); ¹³C NMR

(100 MHz, CDCl₃, DEPT-135) δ 172.5 (C, O=C=O), 165.6 (C, N=C=O), 160.7 (C, C=N), 144.9 (C), 144.8 (2CH), 143.7 (C), 145.0 (C), 144.8 (C), 143.7 (C), 140.6 (C), 140.5 (C), 137.9 (C), 134.4 (C), 132.2 (CH), 132.1 (CH), 129.5 (2CH), 128.8 (2CH), 128.8 (2CH), 128.4 (C), 128.5 (CH), 127.8 (2CH), 127.1 (C), 126.2 (CH), 125.1 (CH), 124.0 (CH), 118.6 (CH), 61.5 (C), 60.4 (CH₂), 56.1 (CH₃), 55.6 (CH), 50.0 (CH₂), 44.8 (CH), 40.1 (CH), 31.9 (CH₂), 31.0 (CH₂), 21.6 (CH₃), 14.2 (CH₃), 14.0 (CH₃); HRMS (ESI) m/z : 768.2714 [M + Na]⁺, calcd for C₄₃H₄₃N₃O₇SNa; Found 768.2714.

Ethyl(*E*)-4-((4*R*,5*R*,6*S*,7*S*)-6-(3-hydroxy-4-methoxyphenyl)-3'-methyl-5'-oxo-1',7-diphenyl-1-tosyl-1,1',2,3,4,5',6,7-octahydrospiro[indole-5,4'-pyrazol]-4-yl)but-2-enoate (5aay**):**

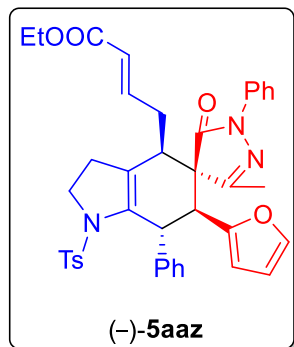
Prepared by following general procedure **D** purified by column chromatography using EtOAc/hexane



and isolated product **5aay** in 73% yield as a brown solid with M. P. 111-113 °C. The enantiomeric excess (*ee*) was determined by chiral stationary phase HPLC using a Daicel Chiralpak IC column (hexane/EtOAc = 70:30, flow rate 0.5 mL/min, λ = 254 nm), t_R = 18.298 min (major), t_R = 23.262 min (minor), $[\alpha]_D^{25}$ = **-103.485** (CHCl₃, **c** = **0.66 g/100mL for 92% ee**); IR (neat) ν_{\max} 3406, 2924, 1699, 1595, 1436, and 1157. cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 8.19 (2H, d, J = 8.2 Hz), 7.83 (2H, d, J = 7.6 Hz), 7.42 (2H, t, J = 8.5 Hz),

7.36 (2H, d, J = 8.1 Hz), 7.22 (1H, t, J = 7.4 Hz), 7.11-7.05 (3H, m), 6.90 (2H, d, J = 6.4 Hz), 6.69 (1H, quin, J = 7.1 Hz), 6.46 (2H, d, J = 7.4 Hz), 5.61 (1H, d, J = 15.4 Hz), 5.33 (1H, br s), 4.80 (1H, d, J = 9.9 Hz), 4.14-4.06 (2H, m), 3.71 (3H, s), 3.70-3.67 (1H, m), 3.58 (1H, ddd, J = 9.2, 9.3, 9.4 Hz), 3.11 (1H, br s), 2.97 (1H, d, J = 10.5 Hz), 2.45 (3H, s), 2.15 (1H, quin, J = 7.7 Hz), 2.01 (3H, s), 1.96-1.84 (2H, m), 1.78-1.68 (2H, m), 1.21 (3H, t, J = 7 Hz); ¹³C NMR (100 MHz, CDCl₃, DEPT-135) δ 172.2 (C, O=C=O), 165.7 (C, N=C=O), 160.6 (C, C=N), 145.8 (C), 145.0 (2CH), 143.6 (C), 140.6 (C), 140.5 (C), 137.7 (C), 134.4 (C), 132.2 (CH), 132.1 (CH), 132.0 (C), 129.6 (C), 129.5 (2CH), 128.8 (3CH), 128.6 (CH), 127.8 (2CH), 127.0 (C), 126.2 (CH), 125.2 (CH), 123.9 (2CH), 119.3 (2CH), 61.5 (C), 60.4 (CH₂), 55.6 (CH₃), 55.5 (CH), 50.0 (CH₂), 44.7 (CH), 40.0 (CH), 31.9 (CH₂), 31.0 (CH₂), 22.6 (CH₃), 14.2 (CH₃), 14.1 (CH₃); HRMS (ESI) m/z : 768.2714 [M + Na]⁺, calcd for C₄₃H₄₃N₃O₇SNa; Found 768.2714.

Ethyl(*E*)-4-((4*R*,5*R*,6*R*,7*S*)-6-(furan-2-yl)-3'-methyl-5'-oxo-1',7-diphenyl-1-tosyl-1,1',2,3,4,5',6,7-octahydrospiro[indole-5,4'-pyrazol]-4-yl)but-2-enoate (5aaz**):**

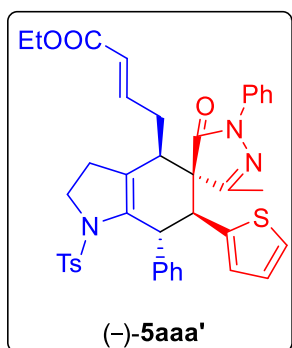


Prepared by following general procedure **D** purified by column chromatography using EtOAc/hexane and isolated product **5aaz** in 78% yield as a brown solid with M. P. 123-125 °C. The enantiomeric excess (*ee*) was determined by chiral stationary phase HPLC using a Daicel Chiralpak IA column (hexane/EtOAc = 70:30, flow rate 0.5 mL/min, λ = 254 nm), t_R = 14.108 min (major), t_R = 20.160 min (minor), $[\alpha]_D^{25}$ = **-90.556** (CHCl₃, **c** = **0.18 g/100mL for 96% ee**); IR (neat) ν_{\max} 2924, 1705, 1597, 1498, 1159

and 752. cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 8.18 (2H, d, J = 8.2 Hz), 7.82 (2H, d, J = 7.6 Hz), 7.43 (2H, t, J = 7.5 Hz), 7.37 (2H, d, J = 8.1 Hz), 7.22 (1H, t, J = 7.4 Hz), 7.16 (2H, d, J = 7.36), 7.06 (1H, d,

$J = 1.5$ Hz), 6.97 (2H, d, $J = 6.5$ Hz), 6.68 (1H, quin, $J = 7.2$ Hz), 6.04 (1H, dd, $J = 1.8, 1.8$), 5.83 (2H, d, $J = 3.16$ Hz), 5.62 (1H, d, $J = 15.4$ Hz), 4.90 (1H, d, $J = 9.84$ Hz), 4.16-4.04 (2H, m), 3.72 (1H, dd, $J = 7.2, 7.3$ Hz), 3.60 (1H, ddd, $J = 9.2, 9.4, 9.3$ Hz), 3.24 (1H, d, $J = 10.6$ Hz), 3.10 (1H, br s), 2.45 (3H, s), 2.16 (1H, quin, $J = 7.9$ Hz), 2.05 (3H, s), 2.03-1.90 (2H, m), 1.77-1.67 (2H, m), 1.21 (3H, t, $J = 7.1$ Hz); ^{13}C NMR (100 MHz, CDCl_3 , DEPT-135) δ 172.6 (C, O-C=O), 166.6 (C, N-C=O), 160.0 (C, C=N), 150.2 (C), 144.6 (2CH), 143.7 (C), 141.8 (C), 140.4 (C), 139.1 (C), 137.8 (C), 134.2 (C), 129.5 (2CH), 128.8 (3CH), 128.7 (CH), 127.9 (2CH), 126.6 (C), 125.2 (CH), 124.1 (CH), 119.0 (3CH), 110.1 (CH), 108.0 (CH), 60.4 (CH_2), 60.2 (C), 50.0 (CH_2), 49.4 (CH), 43.1 (CH), 39.4 (CH), 31.9 (CH_2), 30.9 (CH_2), 21.6 (CH_3), 14.2 (CH_3), 13.6 (CH_3); HRMS (ESI) m/z : 712.2452 $[\text{M} + \text{Na}]^+$, calcd for $\text{C}_{40}\text{H}_{39}\text{N}_3\text{O}_6\text{SNa}$; Found 712.2465.

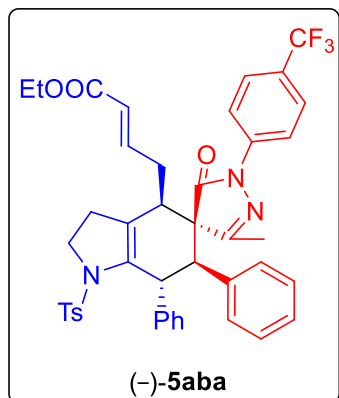
Ethyl(*E*)-4-((4*R*,5*R*,6*R*,7*S*)-3'-methyl-5'-oxo-1',7-diphenyl-6-(thiophen-2-yl)-1-tosyl-1,1',2,3,4,5',6,7-octahydrospiro[indole-5,4'-pyrazol]-4-yl)but-2-enoate (5aaa'**):**



Prepared by following general procedure **D** purified by column chromatography using EtOAc/hexane and isolated product **5aaa'** in 85% yield as a yellow solid with M. P. 120-122 °C. The enantiomeric excess (ee) was determined by chiral stationary phase HPLC using a Daicel Chiralpak IC column (hexane/EtOAc = 70:30, flow rate 0.5 mL/min, $\lambda = 254$ nm), $t_R = 16.356$ min (major), $t_R = 19.423$ min (minor), $[\alpha]_{\text{D}}^{25} = -107.981$ (CHCl_3 , $c = 0.83$ g/100mL for 96% ee); IR (neat) ν_{max} 2926, 1699, 1597, 1498, 1456,

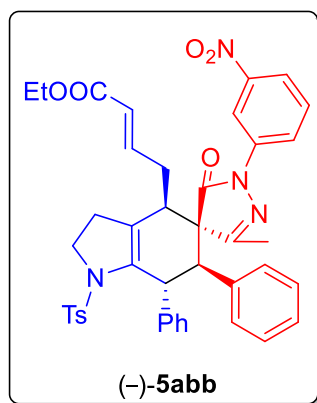
1159 and 688. cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 8.19 (2H, d, $J = 8$ Hz), 7.88 (2H, d, $J = 7.6$ Hz), 7.44 (2H, t, $J = 8.4$ Hz), 7.38 (2H, d, $J = 8.4$ Hz), 7.23 (1H, t, $J = 7.6$ Hz), 7.14-7.10 (2H, m), 6.96-6.93 (3H, m), 6.72-6.65 (2H, m), 6.57 (1H, d, $J = 3.6$ Hz), 5.61 (1H, d, $J = 15.6$ Hz), 4.82 (1H, d, $J = 10.4$ Hz), 4.16-4.04 (2H, m), 3.70 (1H, dd, $J = 7.2, 7.3$ Hz), 3.58 (1H, ddd, $J = 9.2, 9.2, 9.2$ Hz), 3.37 (1H, d, $J = 10.4$), 3.18 (1H, br s), 2.46 (3H, s), 2.15 (1H, quin, $J = 7.2$ Hz), 2.04 (3H, s), 2.03-1.98 (1H, m), 1.95-1.89 (1H, m), 1.75-1.66 (2H, m), 1.21 (3H, t, $J = 7.2$ Hz); ^{13}C NMR (100 MHz, CDCl_3 , DEPT-135) δ 171.7 (C, O-C=O), 165.6 (C, N-C=O), 160.2 (C, C=N), 144.7 (2CH), 143.7 (C), 140.4 (C), 138.8 (C), 137.8 (C), 134.2 (C), 129.5 (2CH), 128.8 (3CH), 128.8 (2CH), 127.9 (2CH), 127.4 (C), 126.6 (CH), 126.4 (CH), 125.8 (C), 125.2 (CH), 124.4 (CH), 124.0 (CH), 119.1 (2CH), 61.5 (C), 60.4 (CH_2), 50.7 (CH), 50.1 (CH_2), 46.2 (CH), 39.8 (CH), 31.9 (CH_2), 31.0 (CH_2), 21.6 (CH_3), 14.2 (CH_3), 13.9 (CH_3); HRMS (ESI) m/z : 728.2223 $[\text{M} + \text{Na}]^+$, calcd for $\text{C}_{40}\text{H}_{39}\text{N}_3\text{O}_5\text{S}_2\text{Na}$; Found 728.2224.

Ethyl(*E*)-4-((4*R*,5*R*,6*S*,7*S*)-3'-methyl-5'-oxo-6,7-diphenyl-1-tosyl-1'-(4-(trifluoromethyl)phenyl)-1,1',2,3,4,5',6,7-octahydrospiro[indole-5,4'-pyrazol]-4-yl)but-2-enoate (5aba**):**



Prepared by following general procedure **D** purified by column chromatography using EtOAc/hexane and isolated product **5aba** in 69% yield as a white solid with M. P. 133-135 °C. The enantiomeric excess (ee) was determined by chiral stationary phase HPLC using a Daicel Chiralpak IC column (hexane/EtOAc = 70:30, flow rate 0.5 mL/min, λ = 254 nm), t_R = 11.002 min (major), t_R = 14.378 min (minor); $[\alpha]_D^{25}$ = -121.667 (CHCl₃, c = 0.11 g/100mL, CHCl₃ for 96% ee); IR (neat) ν_{\max} 2924, 1712, 1654, 1614, 1494, and 1325. cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 8.19 (2H, d, J = 8.2 Hz), 7.99 (2H, d, J = 8.5 Hz), 7.66 (2H, d, J = 8.6 Hz), 7.39 (2H, d, J = 8 Hz), 7.10-7.03 (4H, m), 6.99 (2H, t, J = 7.2 Hz), 6.93-6.79 (3H, m), 6.65 (1H, quin, J = 8.2 Hz), 5.58 (1H, d, J = 15.4 Hz), 4.84 (1H, d, J = 10.32 Hz), 4.11-3.99 (2H, m), 3.75-3.57 (2H, m), 3.18 (1H, br s), 3.09 (1H, d, J = 10.5 Hz), 2.47 (3H, s), 2.22-2.17 (1H, m), 2.06-2.02 (1H, m), 2.01 (3H, s), 1.99-1.94 (1H, m), 1.92-1.67 (2H, m), 1.18 (3H, t, J = 7.1 Hz); ¹³C NMR (100 MHz, CDCl₃, DEPT-135) δ 172.6 (C, O-C=O), 165.5 (C, N-C=O), 161.1 (C, C=N), 144.3 (2CH), 143.8(C), 140.6 (C), 140.3 (C), 140.2 (C), 136.2 (C), 134.4 (C), 129.5(CH), 128.8 (C) 128.7 (2CH), 128.3 (2CH), 127.9 (CH), 127.8 (3CH), 126.9 (C), 126.7 (C, CF₃, q, J = 32.5 Hz), 126.3(CH), 126.1 (2CH, d, J = 4 Hz), 124.1 (2CH), 118.3 (3CH), 61.6 (C), 60.4 (CH₂), 56.3 (CH), 50.0 (CH₂), 44.6 (CH), 40.0 (CH), 32.0 (CH₂), 30.8 (CH₂), 21.6 (CH₃), 14.1 (CH₃), 14.1 (CH₃); HRMS (ESI) m/z : 790.2533 [M + Na]⁺, calcd for C₄₃H₄₀N₃O₅SF₃Na; Found 790.2532.

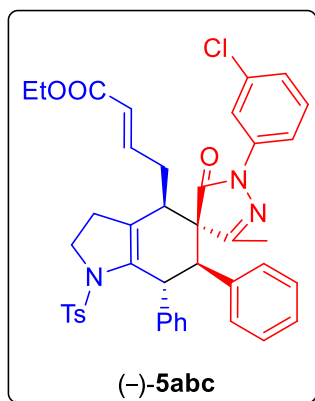
Ethyl(*E*)-4-((4*R*,5*R*,6*S*,7*S*)-3'-methyl-1'-(3-nitrophenyl)-5'-oxo-6,7-diphenyl-1-tosyl-1,1',2,3,4,5',6,7-octahydrospiro[indole-5,4'-pyrazol]-4-yl)but-2-enoate (5abb**):**



Prepared by following general procedure **D** purified by column chromatography using EtOAc/hexane and isolated product **5abb** in 56% yield as a pale-yellow solid with M. P. 112-114 °C. The enantiomeric excess (ee) was determined by chiral stationary phase HPLC using a Daicel Chiralpak IA column (hexane/EtOAc = 70:30, flow rate 0.5 mL/min, λ = 254 nm), t_R = 18.343 min (minor), t_R = 25.241 min (major), $[\alpha]_D^{25}$ = -113.394 (CHCl₃, c = 0.54 g/100mL for 95% ee); IR (neat) ν_{\max} 2926, 1708, 1527, 1597, 1348 and 1157 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 8.73 (1H, t, J = 2.1 Hz), 8.27-8.25 (1H, m), 8.18 (2H, d, J = 8.3 Hz), 8.07-8.04 (1H, m), 7.59 (1H, t, J = 8.2 Hz), 7.41 (2H, d, J = 8 Hz), 7.09-7.03 (4H, m), 6.99 (2H, t, J = 7.6 Hz), 6.93-6.81(3H, m), 6.65 (1H, quin, J = 7.2 Hz), 5.58 (1H, d, J = 15.4 Hz), 4.82 (1H, d, J = 10.4 Hz), 4.11-4.0 (2H, m), 3.78-3.59 (2H, m), 3.20 (1H, br s), 3.10 (1H, d, J = 10.5 Hz), 2.48 (3H, s), 2.22-2.15 (1H, m), 2.03 (3H, s), 2.01-1.97 (1H, m), 1.89-1.79 (1H, m), 1.66 (2H, br s), 1.17 (3H, t, J = 7.2 Hz); ¹³C NMR (100 MHz, CDCl₃, DEPT-135) δ 172.6 (C, O-C=O), 165.4 (C, N-C=O), 161.5 (C, C=N), 148.6 (C), 144.3 (2CH), 143.9 (C), 140.5 (C), 140.2 (C), 138.5 (C), 136.2 (C), 134.4 (C), 129.8 (CH), 129.5 (3CH), 128.7 (3CH), 128.4 (2CH), 128.0 (CH), 127.8 (3CH), 126.5 (C), 126.4 (CH), 124.1 (CH),

123.8 (CH), 119.4 (CH), 113.4 (CH), 61.8 (C), 60.5 (CH₂), 56.3 (CH), 50.0 (CH₂), 44.6 (CH), 40.0 (CH), 32.0 (CH₂), 30.8 (CH₂), 21.7 (CH₃), 14.2 (CH₃), 14.1 (CH₃); HRMS (ESI) *m/z*: 767.2510 [M + Na]⁺, calcd for C₄₂H₄₀N₄O₇Na; Found 767.2509.

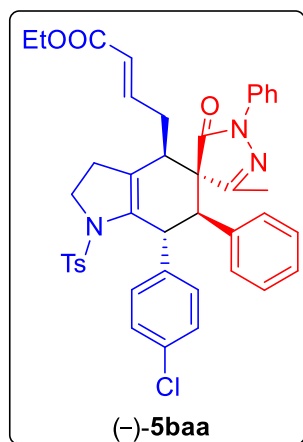
Ethyl(*E*)-4-((4*R*,5*R*,6*S*,7*S*)-1'-(3-chlorophenyl)-3'-methyl-5'-oxo-6,7-diphenyl-1-tosyl-1,1',2,3,4,5',6,7-octahydrospiro[indole-5,4'-pyrazol]-4-yl)but-2-enoate (5abc**):**



Prepared by following general procedure **D** purified by column chromatography using EtOAc/hexane and isolated product **5abc** in 76% yield as a brown solid with M. P. 104-106 °C. The enantiomeric excess (ee) was determined by chiral stationary phase HPLC using a Daicel Chiralpak IC column (hexane/EtOAc = 70:30, flow rate 0.5 mL/min, λ = 254 nm), *t_R* = 15.510 min (major), *t_R* = 21.719 min (minor), [α]_D²⁵ = -101.488 (CHCl₃, c = 0.33 g/100mL for 88% ee); IR (neat) ν_{max} 2924, 2360, 1708, 1593, 1481 and 732 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 8.18 (2H, d, *J* = 8.2 Hz), 7.84 (1H, t, *J* = 1.9 Hz), 7.81-7.78 (1H, m), 7.39 (2H, d, *J* = 8 Hz), 7.33 (1H, t, *J* = 8.1 Hz), 7.18-7.16 (1H, m), 7.07-6.98 (6H, m), 6.88-6.86 (3H, m), 6.65 (1H, quin, *J* = 7.2 Hz), 5.60 (1H, d, *J* = 15.4 Hz), 4.84-4.81 (1H, m), 4.13-4.05 (2H, m), 3.74-3.55 (2H, m), 3.16 (1H, br s), 3.08 (1H, d, *J* = 10.5 Hz), 2.46 (3H, s), 2.44-2.39 (1H, m), 2.20-2.12 (1H, m), 2.03-2.01 (1H, m), 1.98 (3H, s), 1.96-1.92 (1H, m), 1.82-1.73 (1H, m), 1.19 (3H, t, *J* = 7.1 Hz); ¹³C NMR (100 MHz, CDCl₃, DEPT-135) δ 172.3 (C, O=C=O), 165.5 (C, N=C=O), 160.9 (C, C=N), 144.5 (2CH), 143.8 (C), 140.4 (C), 140.3 (C), 138.7 (C), 136.3 (C), 134.5 (C), 134.4 (C), 129.9 (CH), 129.5 (3CH), 128.7 (3CH), 128.3 (CH), 127.8 (CH), 127.7 (3CH), 127.0 (C), 126.3 (CH), 125.0 (CH), 124.1 (CH), 118.8 (CH), 116.7 (2CH), 61.5 (C), 60.4 (CH₂), 56.2 (CH), 50.0 (CH₂), 44.6 (CH), 39.9 (CH), 32.0 (CH₂), 30.8 (CH₂), 21.7 (CH₃), 14.2 (CH₃), 14.0 (CH₃); HRMS (ESI) *m/z*: 756.2269 [M + Na]⁺, calcd for C₄₂H₄₀ClN₃O₅Na; Found 756.2270.

Ethyl(*E*)-4-((4*R*,5*R*,6*S*,7*S*)-7-(4-chlorophenyl)-3'-methyl-5'-oxo-1',6-diphenyl-1-tosyl-1,1',2,3,4,5',6,7-octahydrospiro[indole-5,4'-pyrazol]-4-yl)but-2-enoate (5baa**):**

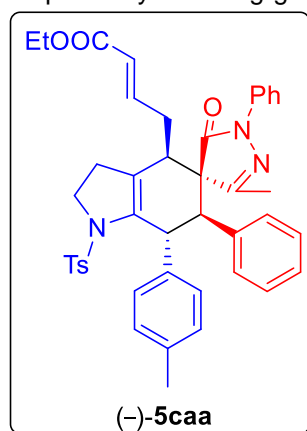
Prepared by following general procedure **D** purified by column chromatography using EtOAc/hexane and isolated product **5baa** in 67% yield as a yellow solid with M. P. 113-115 °C. The enantiomeric excess (ee) was determined by chiral stationary phase HPLC using a Daicel Chiralpak IC column (hexane/EtOAc = 70:30, flow rate 0.5 mL/min, λ = 254 nm), *t_R* = 9.872 min (major), *t_R* = 14.363 min (minor), [α]_D²⁵ = -121.0 (CHCl₃, c = 0.08 g/100mL for 97% ee); IR (neat) ν_{max} 2922, 1720, 1695, 1597, 1456 and 677 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 8.2 (2H, d, *J* = 8.2 Hz), 7.78 (2H, d, *J* = 7.5 Hz), 7.44-7.38 (4H, m), 7.22 (1H, t, *J* = 7.4 Hz), 7.1-6.99 (6H, m), 6.81-6.79 (2H, m), 6.68 (1H, quin, *J* = 7 Hz), 5.62 (1H, d, *J* = 15.5 Hz), 4.87-4.84 (1H, m), 4.13-4.05 (2H, m), 3.74-3.55 (2H, m), 3.13 (1H, br s), 3.01 (1H, d, *J* = 10.5 Hz), 2.47



(3H, s), 2.43-2.37 (1H, m), 2.2-2.13 (1H, m), 2.05-2.02 (1H, m), 2.0 (3H, s), 1.96-1.92 (1H, m), 1.8-1.71 (1H, m), 1.2 (3H, t, $J = 7.1$ Hz); ^{13}C NMR (100 MHz, CDCl_3 , DEPT-135) δ 172.0 (C, O-C=O), 165.6 (C, N-C=O), 160.1 (C, C=N), 144.6 (2CH), 143.8 (C), 140.0 (C), 139.1 (C), 137.6 (C), 136.1 (C), 134.2 (C), 131.9 (C), 129.5 (3CH), 128.8 (3CH), 128. (3CH), 128.4 (CH), 128.0 (2CH), 127.9 (CH), 127.3 (C), 125.3 (CH), 124.0 (CH), 119.13 (3CH), 61.3 (C), 60.4 (CH_2), 56.1 (CH), 50.0 (CH_2), 44.0 (CH), 40.0 (CH), 31.8 (CH_2), 31.0 (CH_2), 21.6 (CH_3), 14.2 (CH_3), 14.0 (CH_3); HRMS (ESI) m/z : 756.2269 $[\text{M} + \text{Na}]^+$, calcd for $\text{C}_{42}\text{H}_{40}\text{ClN}_3\text{O}_5\text{SNa}$; Found 756.2277.

Ethyl(*E*)-4-((4*R*,5*R*,6*S*,7*S*)-3'-methyl-5'-oxo-1',6-diphenyl-7-(*p*-tolyl)-1-tosyl-1',1',2,3,4,5',6,7-octahydrospiro[indole-5,4'-pyrazol]-4-yl)but-2-enoate (5caa**):**

Prepared by following general procedure **D** purified by column chromatography using EtOAc/hexane

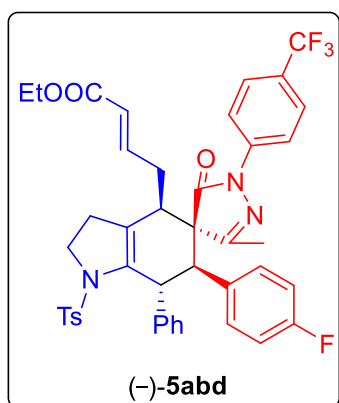


and isolated product **5caa** in 59% yield as a brown solid with M. P. 114-116 °C. The enantiomeric excess (ee) was determined by chiral stationary phase HPLC using a Daicel Chiralpak IC column (hexane/EtOAc = 70:30, flow rate 0.5 mL/min, $\lambda = 254$ nm), $t_R = 10.891$ min (major), $t_R = 16.790$ min (minor), $[\alpha]_D^{25} = -125.076$ (CHCl_3 , $c = 0.33\text{g}/100\text{mL}$ for 97% ee); IR (neat) ν_{max} 2924, 1699, 1597, 1498 and 1159 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 8.2 (2H, d, $J = 8.2$ Hz), 7.78 (2H, d, $J = 7.6\text{Hz}$), 7.43-7.36 (4H, m), 7.21 (1H, t, $J = 7.4$ Hz), 7.07-6.99 (4H, m), 6.87-6.86 (2H, m), 6.76-6.66 (3H, m), 5.61 (1H, d, $J = 15.4$ Hz), 4.83-4.80 (1H, m), 4.15-4.03 (2H, m), 3.73-3.55 (2H, m), 3.13 (1H, br s), 3.07 (1H, d, $J = 10.5$ Hz), 2.46 (3H, s), 2.19 (3H, s), 2.18-2.12 (1H, m), 2.05-2.01 (1H, m), 2.0 (3H, s), 1.95-1.91 (1H, m), 1.79-1.69 (2H, m), 1.2 (3H, t, $J = 7.1$ Hz);

^{13}C NMR (100 MHz, CDCl_3 , DEPT-135) δ 172.1 (C, O-C=O), 165.6 (C, N-C=O), 160.3 (C, C=N), 144.9 (2CH), 143.6 (C), 140.7 (C), 137.6 (C), 137.3 (C), 136.6 (C), 135.5 (C), 134.5 (C), 129.4 (2CH), 128.8 (4C), 128.5 (2CH), 128.2 (CH), 127.7 (CH), 126.8 (C), 125.2 (CH), 123.9 (CH), 119.2 (2CH), 61.5 (C), 60.4 (CH_2), 56.2 (CH), 50.0 (CH_2), 44.1 (CH), 40.0 (CH), 31.9 (CH_2), 30.9 (CH_2), 21.6 (CH_3), 21.1 (CH_3), 14.2 (CH_3), 14.0 (CH_3); HRMS (ESI) m/z : 736.2816 $[\text{M} + \text{Na}]^+$, calcd for $\text{C}_{43}\text{H}_{43}\text{N}_3\text{O}_5\text{SNa}$; Found 736.2816.

Ethyl(*E*)-4-((4*R*,5*R*,6*S*,7*S*)-6-(4-fluorophenyl)-3'-methyl-5'-oxo-7-phenyl-1-tosyl-1'-(4-(trifluoromethyl)phenyl)-1',1',2,3,4,5',6,7-octahydrospiro[indole-5,4'-pyrazol]-4-yl)but-2-enoate (5abd**):**

Prepared by following general procedure **D** purified by column chromatography using EtOAc/hexane



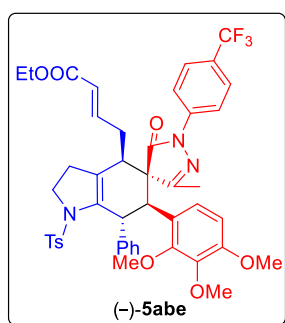
and isolated product **5abd** in 70% yield as a white solid with M. P. 172-175 °C. The enantiomeric excess (ee) was determined by chiral stationary phase HPLC using a Daicel Chiralpak IC column (hexane/EtOAc = 75:25, flow rate 0.5 mL/min, λ = 254 nm), t_R = 12.870 min (major), t_R = 18.881 min (minor); $[\alpha]_D^{25}$ = -95.385 (CHCl₃, c = 0.85 g/100mL for 99.9% ee); IR (neat) ν_{\max} 2924, 1712, 1614, 1512, 1157

and 1325. cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 8.17 (2H, d, J = 8.2 Hz), 8.0 (2H, d, J = 8.5 Hz), 7.67 (2H, d, J = 8.6 Hz), 7.39 (2H, d, J = 8 Hz), 7.09-7.07 (3H, m), 6.87-6.85 (3H, m), 6.72-6.59 (3H, m), 5.58 (1H, d, J

= 15.4 Hz), 4.79-4.77 (1H, m), 4.11-3.99 (2H, m), 3.75-3.56 (2H, m), 3.18 (1H, br s), 3.09 (1H, d, J = 10.5 Hz), 2.47 (3H, s), 2.22-2.14 (1H, m), 2.06-2.03 (1H, m), 2.01 (3H, s), 1.98-1.93 (1H, m), 1.84-1.74 (1H, m), 1.65-1.60 (1H, m), 1.16 (3H, t, J = 7.1 Hz); ¹³C NMR (100 MHz, CDCl₃, DEPT-135) δ 172.5 (C, O-C=O), 165.4 (C, N-C=O), 162.1 (C, C-F, d, J = 245.4 Hz), 161.0 (C, C=N), 144.1 (2CH), 143.9 (C), 140.4 (C), 140.2 (C), 140.1 (C), 134.3 (C), 131.2 (C), 131.2 (C), 129.5 (2CH), 128.8 (CH), 128.7 (2CH), 127.9 (2CH), 126.9 (C), 126.7 (C-CF₃, q, J = 32.5 Hz), 126.4 (CH), 126.1 (2CH, d, J = 4 Hz), 124.1 (2CH), 118.3 (3CH), 115.3 (2CH, d, J = 21 Hz), 61.5 (C), 60.4 (CH₂), 55.5 (CH), 50.0 (CH₂), 44.8 (CH), 39.9 (CH), 32.0 (CH₂), 30.7 (CH₂), 21.6 (CH₃), 14.1 (CH₃), 14.1 (CH₃); HRMS (ESI) m/z : 808.2439 [M + Na]⁺, calcd for C₄₃H₃₉N₃O₅SF₄Na; Found 808.2438

Ethyl(E)-4-((4*R*,5*R*,6*S*,7*S*)-3'-methyl-5'-oxo-7-phenyl-1-tosyl-1'-(4 (trifluoromethyl) phenyl)-6-(2,3,4-trimethoxyphenyl)-1,1',2,3,4,5',6,7-octahydrospiro[indole-5,4'-pyrazol]-4-yl)but-2-enoate (5abe**):**

Prepared by following general procedure **D** purified by column chromatography using EtOAc/hexane



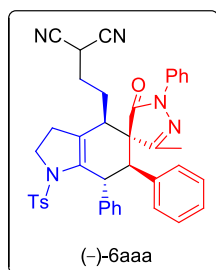
and isolated product **5aba** in 81% yield as a white solid with M. P. 175-180 °C. The enantiomeric excess (ee) was determined by chiral stationary phase HPLC using a Daicel Chiralpak IC column (hexane/EtOAc = 75:25, flow rate 0.5 mL/min, λ = 254 nm), t_R = 15.239 min (major), t_R = 24.042 min (minor); $[\alpha]_D^{25}$ = -119.875 (CHCl₃, c = 0.8 g/100 mL for 98% ee); IR (neat) ν_{\max} 2941, 1722, 1705, 1610, 1498, 1321, and 1157. cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 8.19 (2H, d, J = 8.2 Hz), 8.01 (2H, d, J = 8.5 Hz), 7.66 (2H, d, J = 8.6 Hz), 7.39 (2H, d, J = 8 Hz), 7.09-7.01 (4H, m), 6.92 (1H, br s), 6.65 (1H, quin, J =

6.8 Hz), 6.38 (1H, d, J = 8.9 Hz), 5.58 (1H, d, J = 15.4 Hz), 4.78-4.75 (1H, m), 4.12-3.98 (2H, m), 3.79 (1H, d, J = 10.6 Hz), 3.75-3.72 (1H, m), 3.7 (3H, s), 3.67 (3H, s), 3.65-3.61 (1H, m), 3.23 (1H, br s), 2.8 (3H, s), 2.46 (3H, s), 2.19-2.11 (1H, m), 2.06 (3H, s), 2.04-1.98 (2H, m), 1.96-1.74 (2H, m), 1.17 (3H, t, J = 7.1 Hz); ¹³C NMR (100 MHz, CDCl₃, DEPT-135) δ 173.1 (C, O-C=O), 165.5 (C, N-C=O), 163.3 (C, C=N), 152.8 (C), 151.4 (C), 144.6 (2CH), 143.7(C), 141.5 (C), 140.8 (C), 140.5 (C), 134.6 (C), 129.5 (2CH), 128.6(2CH), 127.8 (2CH), 126.9 (C), 126.4 (C, -CF₃, q, J = 32.5 Hz), 126.3 (CH), 125.9 (2CH, q, J = 4 Hz), 125.5 (C), 123.9 (2CH), 122.5 (C), 121.9 (CH), 118.3 (2CH), 106.9 (CH), 61.9 (C), 60.4

(CH₃), 60.3 (CH₂, CH₃), 55.7 (CH₃), 49.8 (CH₂), 46.1 (CH), 44.8 (CH), 40.09 (CH), 31.9 (CH₂), 30.7 (CH₂), 21.6 (CH₃), 14.1 (CH₃), 13.4 (CH₃); HRMS (ESI) *m/z*: 880.2850 [M + Na]⁺, calcd for C₄₆H₄₆N₃O₈SF₃Na; Found 880.2841.

2-((4*R*,5*R*,6*S*,7*S*)-3'-methyl-5'-oxo-1',6,7-triphenyl-1-tosyl-1,1',2,3,4,5',6,7-octahydrospiro[indole-5,4'-pyrazol]-4-yl)ethyl)malononitrile (6aaa):

Prepared by following general procedure **E** purified by column chromatography using EtOAc/hexane and isolated product **6aaa** in 80% yield as a yellow solid with M. P. 148-150 °C.

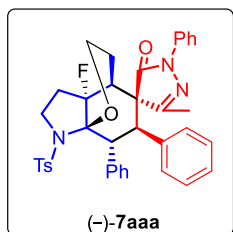


$[\alpha]_D^{25} = -139.000$ (CHCl₃, *c* = 0.1 g/100ml); IR (neat) ν_{\max} 2924, 1693, 1597, 1492 and 1159 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 8.20 (2H, d, *J* = 8.2 Hz), 7.75 (2H, d, *J* = 7.6 Hz), 7.47-7.43 (2H, m), 7.38 (2H, d, *J* = 7.9 Hz), 7.29-7.27 (1H, m), 7.09-6.98 (7H, m), 6.88-6.86 (3H, m), 4.87-4.85 (1H, m), 3.81-3.61 (2H, m), 3.48 (1H, t, *J* = 6.5 Hz), 3.12-3.06 (2H, m), 2.45 (3H, s), 2.10-2.03 (1H, m), 2.01 (3H, s), 1.97-1.89 (2H, m), 1.86-1.74 (3H, m); ¹³C NMR (100 MHz, CDCl₃, DEPT-135)

δ 172.4 (C, N-C=O), 161.0 (C, C=N), 144.3 (C), 141.5 (C), 140.3 (C), 137.5 (C), 136.2 (C), 134.1 (C), 129.7 (3CH), 129.2 (3CH), 128.9 (3CH), 128.5 (CH), 128.0 (CH), 127.9 (3CH), 126.6 (C), 126.5 (CH), 125.9 (CH), 119.6 (3CH), 112.0 (C, CN), 111.8 (C, CN), 61.3 (C), 56.5 (CH), 50.0 (CH₂), 44.5 (CH), 39.7 (CH), 30.6 (CH₂), 28.6 (CH₂), 26.3 (CH₂), 22.9 (CH), 21 (CH₃), 14.2 (CH₃); HRMS (ESI) *m/z*: 702.250 [M + Na]⁺, calcd for C₄₁H₃₇N₅O₃SNa; Found 702.2508.

(3*a*'*R*,4*S*,4'*S*,6'*R*,7'*R*,7*a*'*R*)-3*a*'-fluoro-3-methyl-1,6',7'-triphenyl-1'-tosyl-2',3',3*a*',4',6',7'-hexahydro-1'H-spiro[pyrazole-4,5'-[7*a*,4](epoxyethano)indol]-5(1*H*)-one (7aaa):

Prepared by following general procedure **F** purified by column chromatography using EtOAc/hexane



and isolated product **7aaa** in 75% yield as a white solid with M. P. 95-100 °C. The enantiomeric excess (*ee*) was determined by chiral stationary phase HPLC using a Daicel Chiralpak IC column (hexane/EtOAc = 70:30, flow rate 0.5 mL/min, λ = 254 nm), *t_R* = 19.388 min (major), *t_R* = 30.762 min (minor), $[\alpha]_D^{25} = -123.077$ (CHCl₃, *c* = 0.13 g/100ml for 92%*ee*); IR (neat) ν_{\max} 2924, 1705, 1597, 1496, 1342 and 1159 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.27-7.26 (1H, m), 7.24-7.16 (6H, m), 7.07-6.95 (12H, m), 4.83-4.81 (1H, m), 4.59 (1H, d, *J* = 11.6 Hz), 3.84-3.76 (3H, m), 3.54-3.47 (1H, m), 2.84-2.81 (1H, m), 2.79-2.62 (1H, m), 2.34 (3H, s), 2.32 (3H, d, *J* = 5.12 Hz), 2.23-2.21 (1H, m), 2.18-2.09 (1H, m), 2.03-1.93 (1H, m); ¹³C NMR (100 MHz, CDCl₃, DEPT-135) δ 171.9 (C, N-C=O), 162.1 (C, C=N), 143.0 (C), 142.2 (C), 136.9 (C), 136.6 (C), 135.7 (C), 131.1 (CH), 129.9 (CH), 128.9 (2CH), 128.4 (2CH), 128.2 (2CH), 127.7 (2CH), 127.5 (CH), 127.4 (2CH), 125.8 (CH), 125.3 (CH), 120.0 (3CH), 108.4 (C, d, *J* = 187.51 Hz), 97.0 (C, d, *J* = 19.9 Hz), 62.4 (C), 59.7 (CH₂), 54.6 (CH), 51.5 (CH, d, *J* = 9.82 Hz), 47.1 (CH₂), 36.2 (CH, C-F, d, *J* = 17.9 Hz), 31.5 (CH₂, d, *J* = 26.4 Hz), 28.5 (CH₂, d, *J* = 7.8 Hz), 21.6 (CH₃), 14.1 (CH₃, d, *J* = 4.0 Hz); HRMS (ESI) *m/z*: 672.2303 [M + Na]⁺, calcd for C₃₈H₃₆N₃O₄SFNa; Found 672.2303.

Crystal Structure of **5aai**

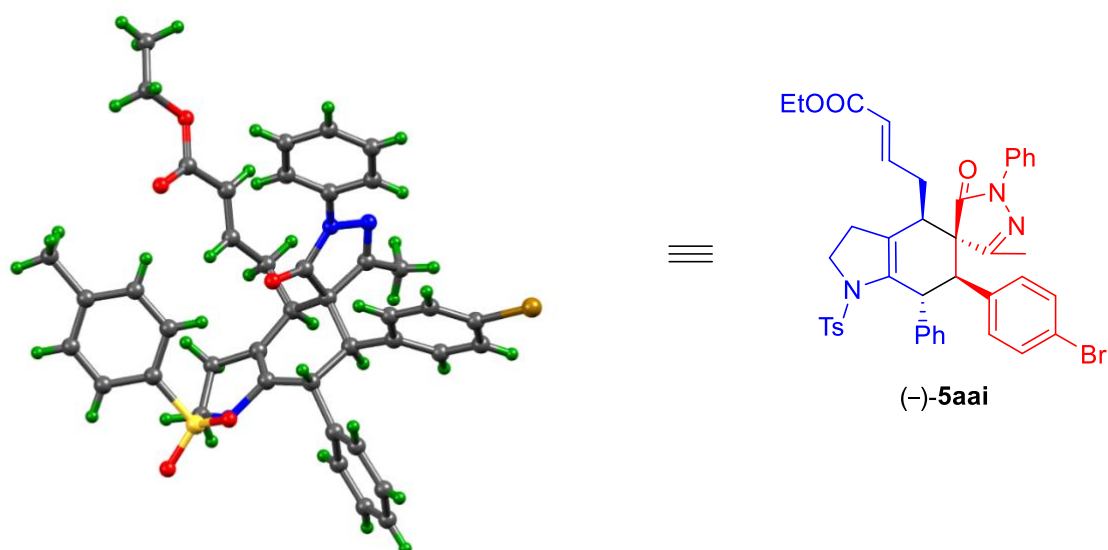


Table 1: Crystal data and structure refinement for **5aai**.

Identification code	shelx	
Empirical formula	C ₄₂ H ₄₀ Br N ₃ O ₅ S	
Formula weight	778.74	
Temperature	297(2) K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group	P 21 21 21	
Unit cell dimensions	a = 13.659(7) Å	α = 90°.
	b = 17.867(9) Å	β = 90°.
	c = 31.896(16) Å	γ = 90°.
Volume	7784(7) Å ³	
Z	8	
Density (calculated)	1.329 Mg/m ³	
Absorption coefficient	1.157 mm ⁻¹	
F(000)	3232	
Crystal size	0.150 x 0.120 x 0.100 mm ³	
Theta range for data collection	2.428 to 25.000°.	
Index ranges	-16 ≤ h ≤ 16, -21 ≤ k ≤ 20, -37 ≤ l ≤ 37	
Reflections collected	81398	
Independent reflections	13677 [R(int) = 0.1249]	
Completeness to theta = 25.000°	99.7 %	

Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.7361 and 0.5933
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	13677 / 154 / 956
Goodness-of-fit on F^2	1.015
Final R indices [$I > 2\sigma(I)$]	$R_1 = 0.0649$, $wR_2 = 0.1291$
R indices (all data)	$R_1 = 0.1354$, $wR_2 = 0.1580$
Absolute structure parameter	0.040(7)
Extinction coefficient	n/a
Largest diff. peak and hole	0.320 and -0.414 e.Å ⁻³